

2,2''-Dimethoxy-1,1':3',1''-terphenyl as a Novel Protective Group for Low-Coordinated Phosphorus Compounds: The Case of Diphosphenes

Alex S. Ionkin and William J. Marshall

DuPont Central Research and Development, Experimental Station, Wilmington, Delaware
19880-0328

Received 22 February 2003

ABSTRACT: A synthetic approach to *meta*-terphenyls iodides bearing methoxy groups in the 2 and 2'' positions has been described. 2,2''-Dimethoxy-1,1':3',1''-terphenyl groups have been shown to stabilize diphosphenes in solution. The existence of conformers of the diphosphene **7** has also been recorded. © 2003 Wiley Periodicals, Inc. *Heteroatom Chem* 14:360–364, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10162

INTRODUCTION

Bulky carbo-substituted *meta*-terphenyl groups have been used for the stabilization of the diphosphene derivatives [1–3]. The carbo-substituted *meta*-terphenyl substituted diphosphenes have been isolated with yields varying from 20 to 86%, which looks satisfactory from a preparation point of view. The introduction of methoxy groups near the metal center has proved to be of vital importance in late transition-metal catalysis. The small deviations in the size and electronic properties of the *ortho*-substituents, including the methoxy-

group of alpha-diimine Ni(II) complexes, make a considerable impact, for example, on the resulting polyethylene [4]. Methoxy-substituted bisphosphines like 1,3-bis(2,6-dimethoxyphenylphosphino)propane happen to be among the most efficient ligands for copolymerization of ethylene and carbon monoxide [5]. In this report we describe a synthetic approach to the *meta*-terphenyl substituted diphosphenes bearing methoxy-groups, which could be used as ligands for late transition-metal catalytic applications.

RESULTS AND DISCUSSION

A one-pot synthesis of *meta*-terphenyls via a two-aryne sequence was tested to prepare methoxy-substituted *meta*-terphenyl iodides [6–8]. These compounds are necessary synthetic intermediates for building *meta*-terphenyldihalophosphines, which are the precursors to diphosphenes in the synthetic route developed by Yoshifujii [9]. 2,2''-Dimethoxy-1,1':3',1''-terphenyl-2' iodide (**1**) was synthesized fairly easily through the tandem aryne addition of the Grignard reagent prepared from 1-bromo-2-methoxy-benzene to the 1,3-dichloro-2-iodo-benzene **2** (see Scheme 1).

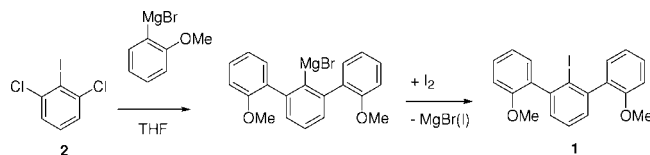
Compound **1** was isolated as a white stable crystalline material, and its structure was proved by X-ray analysis (Fig. 1). As it can be seen from Fig. 1, the two methoxy-phenyl rings are almost perpendicular to the central phenyl ring. The methoxy groups

Correspondence to: Alex S. Ionkin; e-mail: alex.s.ionkin@usa.dupont.com.

Contract grant sponsor: DuPont.

Contract grant number: 8389.

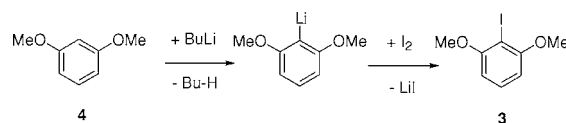
© 2003 Wiley Periodicals, Inc.



SCHEME 1 The route to 2,2''-dimethoxy-1,1':3',1''-terphenyl-2'-iodide (**1**).

are on opposite sides of the molecule and point away from the central ring. Only one conformer of **1**, with a very sharp melting point, was found in the solid state. The situation in the solution was different. The chloroform solution of **1** gave two sets of signals in 1H and ^{13}C NMR spectra. This can be explained by the presence of two stable conformers of **1** in solution. The ratio between the conformers of **1** was about 2:3; and it did not change upon varying the solvent, for example toluene- D_8 instead of $CDCl_3$, or upon increasing the temperature of the toluene- D_8 solution of **1** up to $100^\circ C$. An unambiguous assignment of the structures to each conformer was not possible, as no single important feature stands out from NMR data. There is some literature on the existence of the conformers in alkoxy-substituted terphenyl compounds. Two conformers have been described in the case of an oxacyclophane with terphenyl core [7]. The so-called "up-up" and "up-down" conformers differ by the position of alkoxy groups relative to each other and relative to the aromatic side rings. There are a few calculations describing conformers of terphenyls, resulting from the rotation of aromatic side rings around the central ring [10–12]. The methoxy groups that mainly cause the increase in the energy barrier toward coplanar conformation [10].

To increase the sterical bulk for more efficient protection of diphosphenes, a tetra-methoxy analog of **1** was sought. The starting compound 2-iodo-1,3-dimethoxybenzene (**3**) was prepared by direct lithi-



SCHEME 2 Preparation of 2-iodo-1,3-dimethoxybenzene (**3**).

ation of 1,3-dimethoxybenzene (**4**) and subsequent reaction with iodine [13,14] (Scheme 2).

3.3 equivalents of the Grignard reagent made from **3** were allowed to react with 1 equivalent of **2** according to the standard synthetic protocol for tandem aryne addition of the aryl Grignard reagent, which was followed by quenching with iodine [6–8]. An intended iodine derivative could not be isolated. Instead 2,2'',6,6''-tetramethoxy-1,1':3',1''-terphenyl (**5**) was obtained (see Scheme 3) [7]. The structure of compound **5** was proved by 1H , ^{13}C NMR data, elemental, and X-ray analyses (Fig. 2).

The same phenomenon was observed in attempts to synthesize terphenyl iodide with bulky 2,4,6-tri-*tert*-butylphenyl groups [15], (instead of the 2,6-dimethoxyphenyl group that we used). The authors cited possible steric reasons for the failure to produce the desired iodine derivative and this can be the explanation in our case too. The self-capture mode of an aryne formed from 1,3-dimethoxy magnesium iodide might be a second possibility for the formation of **5**. An analogous path for the preparation of the 2,2'',6,6''-tetrachloro-1,1':3',1''-terphenyl has already been published [8,16]. The report that the Grignard reagent formed from 2-bromo-1,3-dimethoxybenzene was stable in the condition of the same tandem aryne addition [7] implies that we are leaning toward the sterical reason for explaining the failure to produce the desired iodide in the above reaction.

Since only the moderately bulky terphenyl iodide **1** was isolated, we proceeded with this derivative. The lithiation of **1** was carried out by the butyllithium in hexanes. The 2'-dichlorophosphino-2,2''-dimethoxy-1,1':3',1''-terphenyl **6** was prepared by the reaction of above terphenyllithium reagent with phosphorus(III) chloride (Scheme 4). The ^{31}P

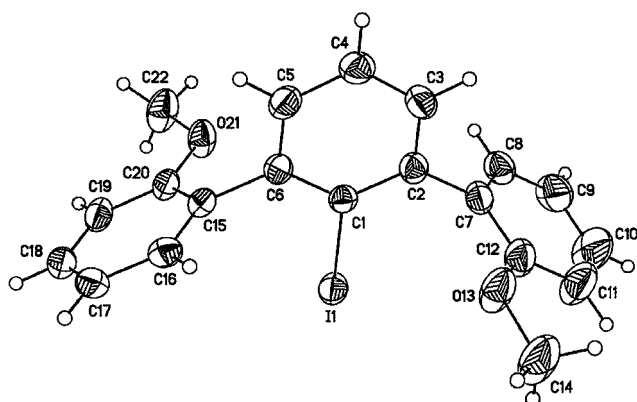
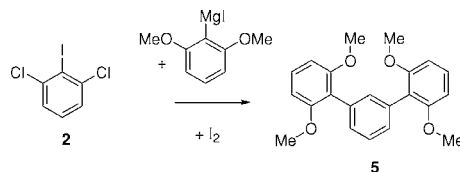
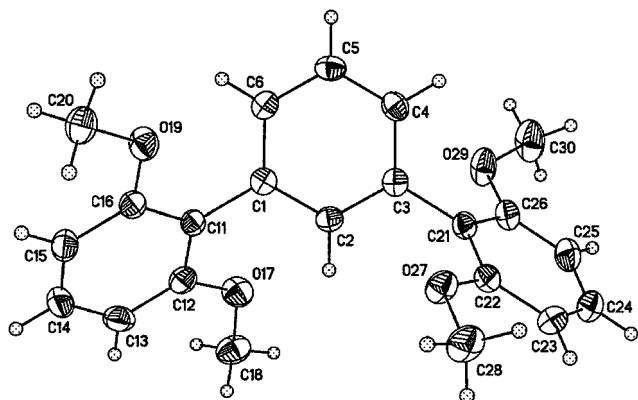


FIGURE 1 ORTEP drawing of **1**.



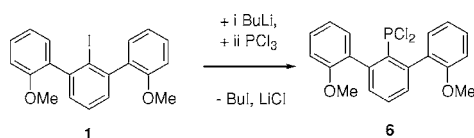
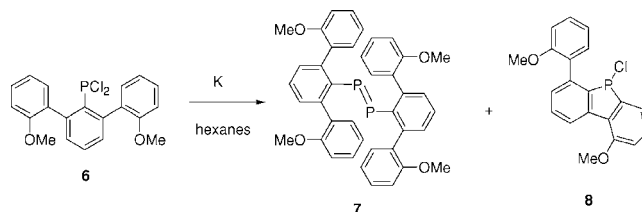
SCHEME 3 Formation of 2,2'',6,6''-tetramethoxy-1,1':3',1''-terphenyl (**5**).

FIGURE 2 ORTEP drawing of **5**.

NMR spectrum of **6** showed two close singlets at $\delta = 160.7$ and 160.6 , with a ratio of about 2:3. As discussed with parent iodide **1**, the existence of two conformers of compound **6** is obvious. Dechlorination of **6** was performed by potassium in hexanes (see Scheme 5). The use of magnesium has been reported to cause complete *ortho*-phosphorylation in carbo-substituted *meta*-terphenyl dichlorophosphines [1].

The orange color attributed to the diphosphene species built up gradually in the above reaction. It took 2 days for complete conversion of the starting dichloride **6** to the mixture of **7** and **8**. The conformers of the diphosphene **7** have chemical shifts in ^{31}P NMR spectrum at $\delta = 510.4$ and 505.7 with a ratio of about 1:2. Such downfield shifts are characteristic for trans orientation of the substituents in the diphosphene moiety [17]. The conformers of the fused cyclic phosphorus compound **8** have chemical shifts in ^{31}P NMR spectrum at $\delta = 129.4$ and 127.6 with a ratio of about 3:1. The *ortho*-phosphorylation was the predominant process in above reaction and the ratio between **8** and **7** was 5:2.

The diphosphene **7** was stable in solution for a month. However, the attempts to isolate it in solid form (including the chromatography on silica gel under inert atmosphere) caused its decomposition. Compound **8** was isolated as the corresponding phosphinic acid **9** (Scheme 6). Its structure was proved by NMR data, elemental, and X-ray analyses, (Fig. 3). A crystal of substance **9** suitable for X-ray

SCHEME 4 The path to 2'-dichlorophosphino-2,2''-dimethoxy-1,1':3',1''-terphenyl (**6**).SCHEME 5 The dechlorination of **6**.

analysis was grown from benzene. We did not observe any hydrogen bonding between the oxygen of methoxy groups and hydrogen of phosphinic acid ($\text{P}-\text{O}-\text{H}$), but we did record a hydrogen bond between oxygen of phosphoryl group and acidic hydrogen ($\text{P}-\text{O}-\text{H}$) in the solid state. This hydrogen bonding dimer, although common with carboxylic acid groups, is rarer for phosphinic acids. A search of the Cambridge Crystal Database yielded only three other structures with a similar arrangement [18–20].

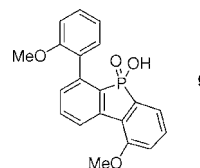
Various unsymmetrical diphosphenes ($\text{R}-\text{P}=\text{P}-\text{R}'$) bearing different protective groups at the phosphorus atoms have been described [21]. To our knowledge this is the first case of the observation of conformers in diphosphenes. The rotational isomers in low-coordinated phosphorus chemistry have been noted in the family of 1,4-diphospha-1,3-butadienes [22]. The application of **1** for the stabilization of other low-coordinated phosphorus compounds is in progress.

The CCDC contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk). The deposition numbers are CCDC 202908, 202907, and 202909 for **1**, **5**, and **9** respectively.

EXPERIMENTAL

2,2''-Dimethoxy-1,1':3',1''-terphenyl-2' Iodide (**1**)

To Grignard reagent prepared freshly from 68.54 g (0.3665 mol) 1-bromo-2-methoxy-benzene and 10.55 g (0.4341 mol) of magnesium turnings in

SCHEME 6 1-Methoxy-6-(2-methoxy-phenyl)-5-oxo-5H-5λ⁵-dibenzophosphol-5-ol (**9**).

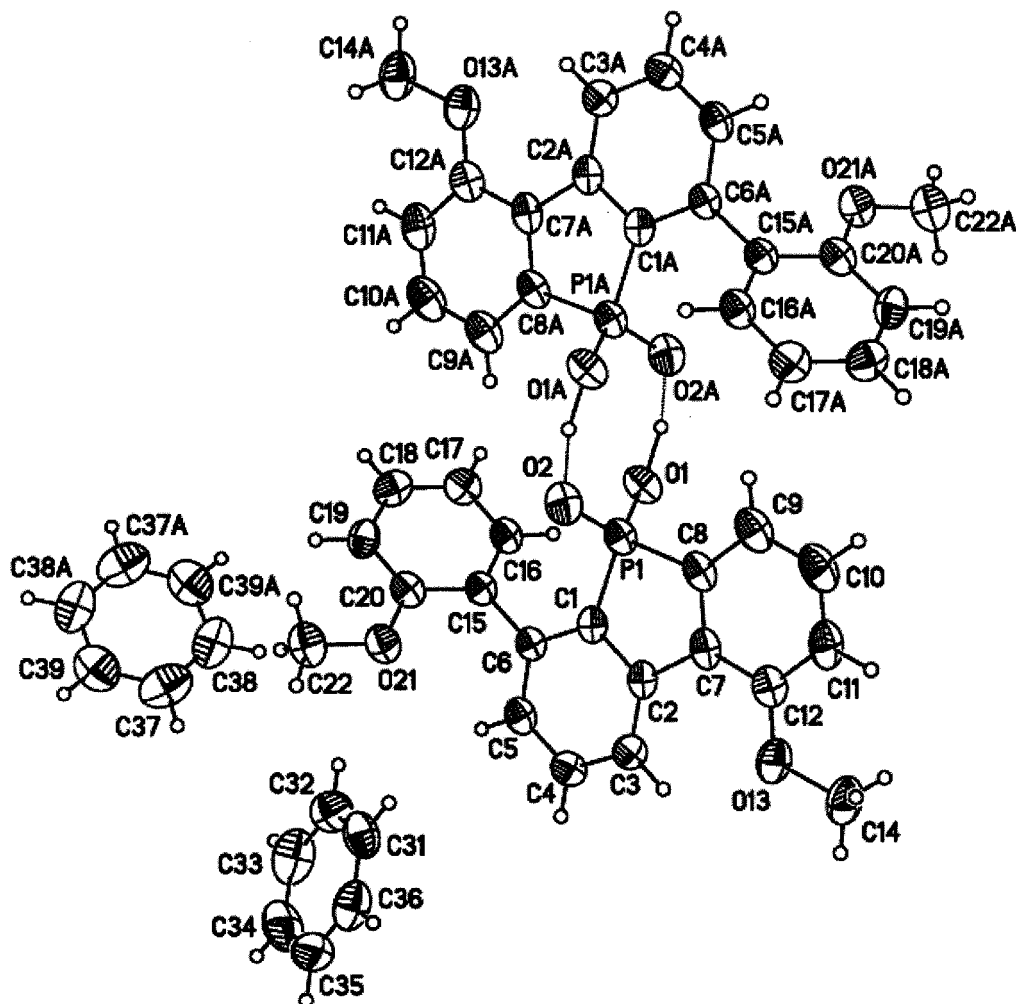


FIGURE 3 ORTEP drawing of $(9)_2 \cdot (C_6H_6)_2$.

300 ml of THF was added the solution of 25.0 g (0.0916 mol) of 1,3-dichloro-2-iodo-benzene (**2**) in 100 ml of THF at room temperature. The reaction mixture was refluxed for 10 h and allowed to cool down to ambient temperature. The solution of 34.4 g (0.1354 mol) of I_2 in 150 ml of THF was added dropwise to the reaction mixture with cooling by water/ice bath. After the mixture was stirred for 12 h at room temperature, a solution of 50.00 g Na_2SO_3 in 250 ml of water was added to destroy the excess iodine and to dissolve the inorganic salts. The organic layer was dried over $MgSO_4$, the solvents removed in vacuum, and the residue was recrystallized from ethyl alcohol. The yield of **1** as a white solid was 28.42 g (75%) with m.p. 128.2°C. 1H NMR ($CDCl_3$) (major conformer) δ = 3.78 (s, 6H, Me), 6.94–7.39 (m, 11H, Ar-H); 1H NMR ($CDCl_3$) (minor conformer) δ = 3.81 (s, 6H, Me), 6.92–7.41 (m, 11H, Ar-H). ^{13}C NMR ($CDCl_3$) (major conformer) δ = 55.58, 106.84, 111.05, 120.26, 127.38,

128.69, 129.16, 130.70, 134.71, 144.84, 156.36. ^{13}C NMR ($CDCl_3$) (minor conformer) δ = 55.64, 107.16, 111.22, 120.32, 127.50, 128.76, 129.18, 130.95, 134.83, 144.84, 156.50. Anal. Calcd. for $C_{20}H_{17}IO_2$: C, 57.71; H, 4.12. Found: C, 57.36; H, 3.83.

2-Iodo-1,3-dimethoxy-benzene (**3**)

One hundred eighty-seven milliliters of 1.7 M solution of butyllithium in hexanes was added dropwise to the solution of 40.0 g (0.2895 mol) of 1,3-dimethoxybenzene (**4**) in 150 ml of ethyl ether containing 0.1 g of tetramethylenediamine at 0°C. The reaction mixture was stirred overnight and 74.0 g (0.2913 mol) of iodine in 150 ml of THF was added again at 0°C. After stirring the mixture overnight, it was poured into saturated aqueous Na_2SO_3 and extracted by 200 ml of ethyl acetate. The organic phase was dried over magnesium sulfate and recrystallized from acetone. The yield of **3** was 66.00 g (86%) with

m.p. 103.8°C. ^1H NMR (CDCl_3) δ = 3.89 (s, 6H, Me), 6.49 (d, 2H, J = 8.0 Hz, Ar-H), 7.25 (d, 1H, J = 8.0 Hz, Ar-H).

2,2'',6,6''-Tetramethoxy-1,1':3',1''-terphenyl (**5**)

To Grignard reagent prepared freshly from 30.00 g (0.1136 mol) **3** and 5.45 g (0.2242 mol) of magnesium turnings in 200 ml of THF was added the solution of 9.40 g (0.0344 mol) of **2** in 100 ml of THF at room temperature. The reaction mixture was refluxed for 10 h and allowed to cool down to ambient temperature. The solution of 31.74 g (0.1250 mol) of I_2 in 150 ml of THF was added dropwise to the reaction mixture with cooling by water/ice bath. After the mixture was stirred for 12 h at room temperature, a solution of 50.00 g Na_2SO_3 in 250 ml of water was added to destroy the excess iodine and to dissolve the inorganic salts. The organic layer was dried over MgSO_4 , the solvents removed in vacuum, and the residue was purified by chromatography on silica gel with the mixture of petroleum ether/ethyl ether 8:2 as an eluent. The yield of **5** as a white solid was 2.78 g (23%) with m.p. 177.5°C. ^1H NMR (CDCl_3) δ = 3.67 (s, 12H, Me), 6.54 (d, J = 8.3 Hz, 4H, Ar-H-3,3'',5,5''), 7.29 (t, J = 8.3 Hz, 2H, Ar-H-4,4'') 7.30–7.50 (m, 4H, central Ar-H). ^{13}C NMR (CDCl_3) δ = 55.75, 104.26, 119.92, 126.51, 128.13, 129.20, 132.78, 133.55, 157.68. Anal. Calcd for $\text{C}_{22}\text{H}_{22}\text{O}_4$: C, 75.41; H, 6.33. Found: C, 75.15; H, 6.32.

1-Methoxy-6-(2-methoxy-phenyl)-5-oxo-5H-5 λ^5 -dibenzophosphol-5-ol (**9**)

Five grams (0.0120 mol) of **1**, 100 ml of hexanes, and 8.5 ml of 1.7 M solution of butyllithium in hexanes were stirred at room temperature for 48 h. Phosphorus(III) chloride (2.75 g, 0.020 mol) was added to the reaction mixture. The reaction mixture was kept at room temperature for an additional 24 h. The solvents were removed under vacuum (0.1 mm) at room temperature and the residue was redissolved in 200 ml of hexanes. The precipitate was filtered off. The ^{31}P NMR spectrum of the filtrate contained only two singlets at δ = 160.7 and 160.6 with ratio about 2:3. It was used as "it is" in the dechlorination step. Small pieces of potassium metal (0.93 g, 0.0238 mol) were placed in the above-prepared solution of the dichlorophosphine **6** at the room temperature with magnetic stirrer in the nitrogen glovebox. After 2 days the mixture was filtered. The solvent was removed in vacuum and the residue was purified by chromatography on silica gel, using benzene as an eluent. Any residual solvent was removed from the product by drying in vacuum at 0.1 mm over night.

The yield of **9** was 2.71 g (64%) as slightly yellow hygroscopic solid with m.p. 93.7°C with decomposition. ^1H NMR (DMSO-d_6) δ = 3.71 (s, 3H, Me), 4.01 (s, 3H, Me), 6.94–8.34 (m, 10H, Ar-H). ^{31}P NMR (DMSO-d_6) δ = 36.3. Anal. Calcd for $\text{C}_{20}\text{H}_{17}\text{O}_4\text{P}$: P, 8.79. Found: P, 8.49.

ACKNOWLEDGMENT

The authors thank Vicki North for assistance with DSC measurements.

REFERENCES

- [1] Twamley, B.; Sofield, C. D.; Olmstead, M. M.; Power, P. P. *J Am Chem Soc* 1999, 121, 3357–3367.
- [2] Urnezis, E.; Protasiewicz, J. D. *Main Group Chem* 1996, 1, 369–372.
- [3] Shah, S.; Burdette, S. C.; Swavey, S.; Urbach, F. L.; Protasiewicz, J. D. *Organometallics* 1997, 16, 3395–3400.
- [4] Schmid, M.; Eberhardt, R.; Klinga, M.; Leskelae, M.; Rieger, B. *Organometallics* 2001, 20, 2321–2330.
- [5] Preparation of phosphide intermediates for polymerization catalysts. *Neth Appl* (1989), 28 pp. NL 8800770.
- [6] Du, C. J. F.; Hart, H.; Ng, K. K. D. *J Org Chem* 1986, 51, 3162–3165.
- [7] Grewal, R. S.; Hart, H.; Vinod, T. K. *J Org Chem* 1992, 57, 2721–2726.
- [8] Saednya, A.; Hart, H. *Synthesis* 1996, 12, 1455–1458.
- [9] Yoshifuji, M.; Shibayama, K.; Inamoto, N.; Matsushita, T.; Nishimoto, K. *J Am Chem Soc* 1983, 105, 2495–2497.
- [10] Pan, J.-F.; Chua, S.-J.; Huang, W. *Thin Solid Films* 2000, 363, 1–5.
- [11] Anariba, F.; McCreery, R. L. *J Phys Chem B* 2002, 106, 10355–10362.
- [12] Chavatte, P.; Yous, S.; Marot, C.; Baurin, N.; Lesieur, D. *J Med Chem* 2001, 44, 3223–3230.
- [13] Bennetau, B.; Rajarison, F.; Dunogues, J.; Babin, P. *Tetrahedron* 1993, 49, 10843–10854.
- [14] Anderson, J. C.; Pearson, D. J. *J Chem Soc, Perkin Trans 1* 1998, 2023–2029.
- [15] Schiemenz, B.; Power, P. P. *Organometallics* 1996, 15, 958–964.
- [16] Kress, T. H.; Leanna, M. R. *Synthesis* 1988, 803–805.
- [17] Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley: New York, 2000; pp. 333–334.
- [18] Reis, A. H.; Peterson, S. W.; Druyan, M. E.; Gebert, E.; Mason, G. W.; Peppard, D. F. *Inorg Chem* 1976, 15, 2748–2752.
- [19] Tkachev, V. V.; *Zh Strukt Khim* 1991, 32, 125–133.
- [20] Kazakov, P. V.; Odinets, I. L.; Antipin, M. Yu.; Petrovskii, P. V.; Kovalenko, L. V.; Struchkov, Yu. T.; Mastryukova, T. A. *Izv Akad Nauk SSSR Ser Khim* 1990, 2120–2127.
- [21] Yoshifuji, M. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M.; Scherer, O. J. (Eds.); Georg Thieme Verlag: Stuttgart, 1990; pp. 321–337.
- [22] Yoshifuji, M.; Ichikawa, Y.; Toyota, K.; Kasashima, E.; Okamoto, Y. *Chem Lett* 1997, 1, 87–88.