Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters 48 (2007) 5665–5668

Tetrahedron Letters

(*R*,*R*,*R*)-Tris(2-hydroxy-1-methylethyl)- and (*S*,*S*,*S*)-tris(2-hydroxy-2-methylethyl)phosphine: water-soluble chiral trialkylphosphines with C_3-symmetry

Peter Kasák,[a,†] Vladimir B. Arion[b] and Michael Widhalm[a,*]

[a]*Institute for Organic Chemistry, University of Vienna, Währinger Straße 38, A-1090 Vienna, Austria*
[b]*Institute of Inorganic Chemistry, University of Vienna, Währinger Straße 42, A-1090 Vienna, Austria*

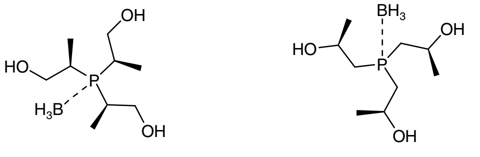
Received 18 April 2007; revised 1 June 2007; accepted 6 June 2007
Available online 9 June 2007

Abstract—The first α- and β-chiral water-soluble trialkylmonophosphines, **1** and **2**, respectively, both with C_3 symmetry, were synthesised from sodium phosphide and chiral mesylates, accessible from (*S*)-ethyl lactate. X-ray structures of a corresponding 2:1 gold(I) complex [$\mathbf{1}_2$Au(I)]OTf and of a borane complex **2**·$\mathbf{BH_3}$ were determined.

In addition to the enormous number of chiral diphosphines discovered to date and employed successfully in asymmetric catalysis, compounds with a single phosphorus(III) centre[1] are also attracting increasing interest. In contrast to (P-chiral) triaryl- or diarylalkylphosphines, phosphites, phosphonites, phosphinites and phosphoramidites, the group of (electron-rich) chiral trialkylphosphines[2] has scarcely been explored.[3] The most popular examples belong to the group of DUPHOS-type ligands.[4] Another subgroup based on tartaric acid and D-mannitol[5] is also of particular interest, since the approach based on the use of carbohydrates as starting material does not require optical resolution procedures or asymmetric synthesis and provides structural diversity. In addition, it often gives rise to phosphines with considerable solubility in water. The latter are highly important for their use in catalysis since they allow the reactions to be conducted in an aqueous phase with a potential to facilitate work-up, reuse of the catalyst and to establish environmentally benign processes.

The benefits of C_2 symmetry for auxiliaries in asymmetric transformations resulting in a reduced number of diastereomorphous transition states usually with better asymmetric induction have been discussed.[6] For monophosphine ligands, the same is true if a (propeller shaped) arrangement with C_3 symmetry is adopted.[7] While tripodal ligands with C_3 symmetry have frequently been reported,[4,8] monophosphines are less common,[9] and to the best of our knowledge, only a single paper has been published dealing with the synthesis of C_3 symmetric monophosphines with chiral benzylic centres attached to P.[10] It seemed therefore desirable to find convenient synthetic routes to chiral hydrophilic trialkylphosphines with C_3 symmetry, preferably using cheap precursors from the chiral pool.

Here we report the synthesis of borane complexes of (*R*,*R*,*R*)-tris(2-hydroxy-1-methylethyl)phosphine **1** and (*S*,*S*,*S*)-tris(2-hydroxy-2-methylethyl)phosphine **2**, respectively (Fig. 1), as outlined in Scheme 1, representing the



1·$\mathbf{BH_3}$ **2**·$\mathbf{BH_3}$

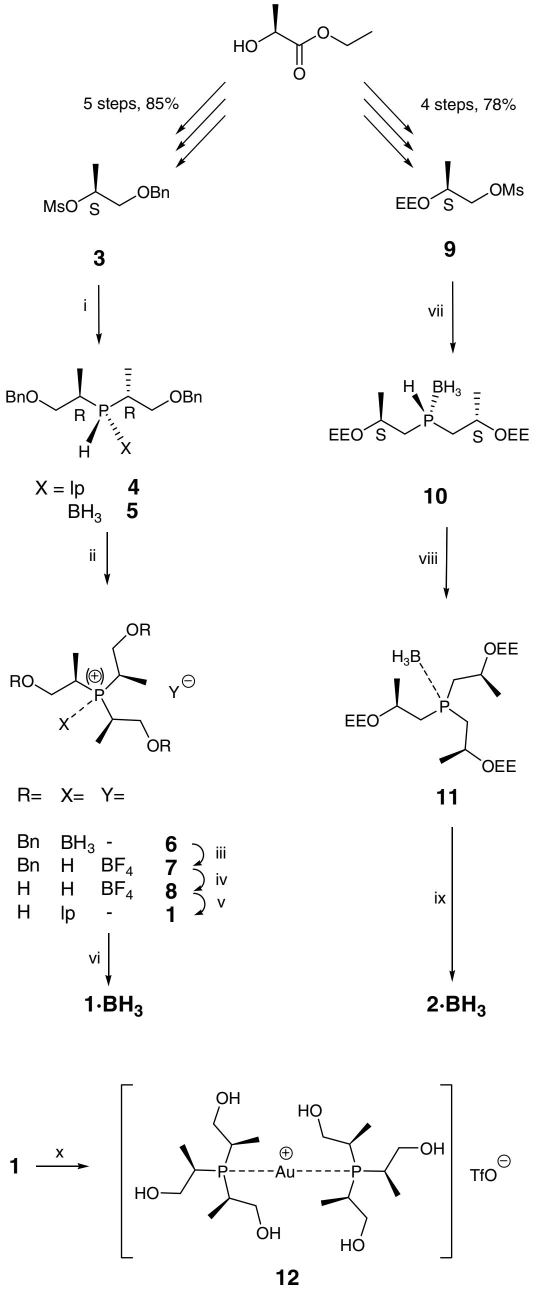
Figure 1. Borane complexes of (*R*,*R*,*R*)-tris(2-hydroxy-1-methylethyl)phosphine (left side) and (*S*,*S*,*S*)-tris(2-hydroxy-2-methylethyl)phosphine (right side).

Keywords: Sodium phosphide; Hydroxyphosphines; Phosphine borane complexes; Gold(I) complex; Chiral ligands.

[*] Corresponding author. Tel.: +43 1 4277 52111; fax: +43 1 4277 9521; e-mail: m.widhalm@univie.ac.at

[†] Present address: Polymer Institute of the Slovak Academy of Sciences, Dúbravská cesta 9, 842 36 Bratislava, Slovakia.

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.06.030



Scheme 1. (i) (a) Na$_3$P/DMF, 0°→40 °C, 10 h; (b) BH$_3$/THF, 0°C→rt, 2 h, 56% (from **3**); (ii) *n*-BuLi/THF, **3**, 0 °C→55 °C, 2 h, 78%; (iii) BF$_4$/CH$_2$Cl$_2$ −10 °C→rt; (iv) Pd–C/H$_2$/EtOH, r.t., 91 h, 92% (from **6**); (v) Amberlyst A21/MeOH, 95%; (vi) BH$_3$/THF, 0 °C→rt, 80%; (vii) (a) Na$_3$P/THF, 0°→30 °C, 10 h; (b) BH$_3$/THF, 0 °C→rt, 30 min, 65% (m.d.); (viii) *n*-BuLi/THF, **9**, 0 °C→30 °C, overnight, 74% (m.d.); (ix) *p*-TsOH (cat)/EtOH, rt, 24 h, 93%; (x) (a) C$_5$H$_{14}$AuCl/MeOH, 76%; (b) AgOTf/MeOH, quant.

simplest molecules of this type.[11] For the synthesis of **1**, the required precursor **3** was accessible from (*S*)-ethyl lactate in five steps following a published procedure[12] (total yield 85%). As a nucleophilic P(III) source, Na$_3$P was found to be the reagent of choice[13] since its preparation from red phosphorus and sodium naphthalenide proceeded safely under argon at rt, requiring no special equipment and avoiding the use of gaseous phosphine.[14] Reaction of Na$_3$P with **3** in dimethylformamide (DMF) yielded 56% of secondary phosphine **4**[15] (isolated as borane complex **5**[16]). It should be noted that neither excess of mesylate nor extended reaction time afforded considerable amounts of the trialkylphosphine and no evidence for partial racemization was found by NMR spectroscopy, which would give rise to the formation of the *meso* isomer. The introduction of the third P-substituent succeeded after activation of **4** as borane complex **5**, which was cleanly deprotonated with *n*-BuLi and alkylated with **3** to yield **6** (78%). While the borane complex **6** could not be debenzylated under standard conditions[17] (H$_2$-Pd/C, H$_2$–Rh/Al$_2$O$_3$, Raney-Ni, Li–naphthalenide), the corresponding phosphonium salt **7** was smoothly debenzylated with H$_2$–Pd/C to give triol **8** (92%) as a yellowish hygroscopic oil, representing an air stable masked phosphine from which **1**[18] was liberated by passing through a short column filled with weakly basic ion exchange resin (95%).[19] Crude phosphine **1** could be further purified by distillation or reprotected as borane complex **1·BH$_3$**. The free phosphine **1** displayed good solubility and stability in water and protic solvents; a NMR sample prepared from 30 mg of **1** in CD$_3$OD/D$_2$O (1:1) under argon remained unchanged for at least 24 h at 30 °C.

From the same starting material, the isomeric β-chiral phosphine borane complex **2·BH$_3$** was also accessible using appropriate protective groups (Scheme 1). Ethoxyethyl protected propan-1,2-diol, which was prepared from (*S*)-ethyl lactate according to Ref. 20, was converted to mesylate **9** under standard conditions and reacted in excess (∼1.5 equiv) with Na$_3$P to afford the secondary phosphine in 65% yield (isolated as borane complex **10**). The activated substrate **10** was smoothly alkylated to yield **11**, and after cleavage of ethoxyethyl groups with TsOH, the borane complex of trihydroxyphosphine **2** was isolated as a crystalline solid in 35% overall yield (from (*S*)-ethyl lactate). Subsequent treatment with Et$_3$N liberated phosphine **2**.

To confirm the proposed structures of **1** and **2**, crystal structure analyses were attempted. Since neither **1**, **1·BH$_3$** nor the corresponding phosphine oxide or precursors **6**–**8** could be obtained in a crystalline form, a cationic gold(I) complex of **1** was synthesised. Reaction of the free ligand with a stoichiometric amount of the precursor *cis*-cyclooctene gold(I) chloride[21] in MeOH afforded a 2:1 complex, $[\mathbf{1}_2\mathrm{Au(I)}]^+\mathrm{Cl}^-$ as the main product as evidenced by NMR and field desorption mass spectrometry (FD-MS) ($m/z = 613.8$, $[\mathrm{M}-\mathrm{Cl}]^+$).[22] The complex displayed high solubility in water and MeOH and its stability in air enabled chromatographic purification on SiO$_2$ in 2-PrOH. Suitable crystals could be obtained for X-ray structure determination after conversion of the chloride to the corresponding triflate $[\mathbf{1}_2\mathrm{Au}]\mathrm{CF_3SO_3}$.[23] The result of X-ray diffraction study of **12** is shown in Figure 2. The compound crystallised in the orthorhombic space group $P2_12_12_1$. The crystal structure consists of cations $[\mathrm{Au}\{\mathrm{P(CHMeCH_2OH)_3}\}_2]^+$ and triflate anions. The gold atom is linearly coordinated by two P(CHMeCH$_2$OH)$_3$ ligands (P1–Au–P2 = 176.87(2)°) with Au–P bond distances of 2.3031(6) and 2.3105(6) Å. These are significantly longer

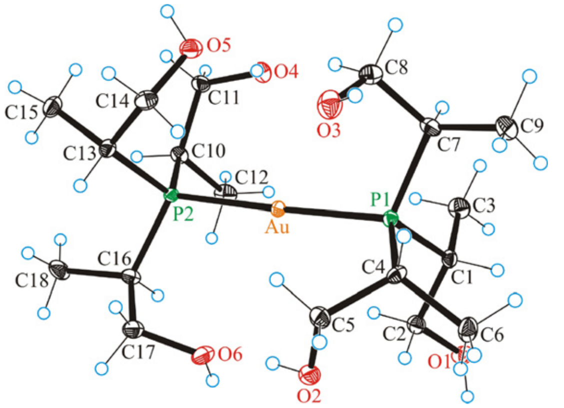


Figure 2. ORTEP plot of the cation $[\mathbf{1}_2\mathrm{Au}]^+$ with atom-numbering scheme. The thermal ellipsoids are drawn at the 50% probability level.

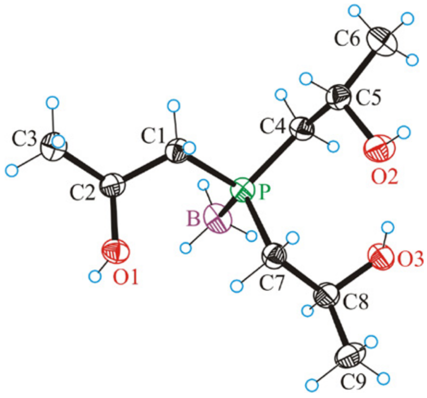


Figure 3. ORTEP plot of **2**·$\mathbf{BH_3}$ with atom-numbering scheme. The thermal ellipsoids are drawn at the 50% probability level.

than that in $Au(PTA)_2Cl$ [PTA = 1,3,5-triaza-7-phosphaadamantane) with 2.261(5) Å[24] and well comparable with those in $[Au\{FcCH_2P(CH_2OH)_2\}_2]Cl$ with Au–P1 2.311(2) Å, Au–P2 2.310(2) Å[25] or $[Au\{PH(t\text{-}Bu)_2\}_2]BF_4$ with Au–P 2.3119(8) Å.[26] In contrast, the β-chiral species **2**·$\mathbf{BH_3}$ showed excellent crystallinity permitting its solid state structure determination (Fig. 3).[27]

In summary, we have discovered a straightforward route to produce α-chiral secondary and tertiary alkyl phosphines from alkylmesylates and sodium phosphide as P-source. This is exemplified by the synthesis of new water-soluble C_3-symmetrical monophosphine borane complexes from (*S*) ethyl lactate. The extension of this concept to the synthesis of further secondary and tertiary alkyl phosphines and their application in asymmetric catalysis is under way and will be reported in due course.

Acknowledgements

P.K. is grateful for a grant provided by *Fonds zur Förderung der wissenschaftlichen Forschung in Österreich* (Lise Meitner Grant No. M852-N11). We are also grateful to Mr A. Roller for the collection of X-ray data.

Supplementary data

The crystal data are available at www.ccdc.cam.ac.uk The CCDC numbers are 637239 for **12** and 642870 for **2**·$\mathbf{BH_3}$. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.06.030.

References and notes

1. Jerphagnon, T.; Renaud, J.-L.; Bruneau, C. *Tetrahedron: Asymmetry* **2004**, *15*, 2101.
2. For electron rich phosphines, see: Valentine, D. H.; Hillhouse, J. H. *Synthesis* **2003**, 2437.
3. (a) Graf, C.-D.; Malan, C.; Harms, K.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 5581; (b) Imamoto, T.; Oohara, N.; Takahashi, H. *Synthesis* **2004**, 1353.
4. (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518; (b) Clark, T. P.; Landis, C. R. *Tetrahedron: Asymmetry* **2004**, *15*, 2123.
5. Castillón, S.; Claver, C.; Diaz, Y. *Chem. Soc. Rev.* **2005**, *34*, 702.
6. Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.
7. (a) Moberg, C. *Angew. Chem.* **1998**, *110*, 260; (b) Gibson, S. E.; Castaldi, M. P. *Chem. Commun.* **2006**, 3045.
8. (a) Castaldi, M. P.; Gibson, S. E.; Rudd, M.; White, A. J. P. *Chem. Eur. J.* **2006**, *12*, 138; (b) Castaldi, M. P.; Gibson, S. E.; Rudd, M.; White, A. J. P. *Angew. Chem., Int. Ed.* **2005**, *44*, 3432; (c) Whitnall, M. R.; Hii (Mimi), K. K.; Thornton-Pett, M.; Kee, T. P. *J. Organomet. Chem.* **1997**, *529*, 35; (d) Baker, M. J.; Pringle, P. G. *Chem. Commun.* **1993**, 314; (e) Sorrell, T. N.; Pigge, F. C.; White, P. S. *Inorg. Chim. Acta* **1993**, *210*, 87; (f) Adolfsson, H.; Wärnmark, K.; Moberg, C. *Chem. Commun.* **1992**, 1054; (g) Tokar, C. J.; Kettler, P. B.; Tolman, W. B. *Organometallics* **1992**, *11*, 2737; (h) Ward, T. R.; Venanzi, L. M.; Albinati, A.; Lianza, F.; Gerfin, T.; Gramlich, V.; Tombo, G. M. R. *Helv. Chim. Acta* **1991**, *74*, 983; (i) Burk, M. J.; Harlow, R. L. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1462.
9. (a) You, J.; Wróblewski, A. E.; Verkade, J. G. *Tetrahedron* **2004**, *60*, 7877; (b) Powell, M. T.; Porte, A. M.; Reibenspies, J.; Burgess, K. *Tetrahedron* **2001**, *57*, 5027; (c) Pickett, T. E.; Richards, C. J. *Tetrahedron Lett.* **2001**, *42*, 3767; (d) Langer, F.; Knochel, P. *Tetrahedron Lett.* **1995**, *36*, 4591; (e) Bolm, C.; Sharpless, K. B. *Tetrahedron Lett.* **1988**, *29*, 5101; (f) Bolm, C.; Davies, W. M.; Halterman, R. L.; Sharpless, K. B. *Angew. Chem.* **1988**, *100*, 882.
10. Wyatt, P.; Eley, H.; Charmant, J.; Daniel, B. J.; Kantacha, A. *Eur. J. Org. Chem.* **2003**, 4216.
11. For the synthesis of the analogous triethanolamine from (*S*) ethyl lactate, see: Stachel, S. J.; Ziller, J. W.; Van Vranken, D. L. *Tetrahedron Lett.* **1999**, *40*, 5811.
12. (a) Buchwald, S. L.; Pliura, D. H.; Knowles, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 4916; (b) Brunsveld, L.; Zhang, H.; Glasbeek, M.; Vekemans, J. A. J. M.; Meijer, E. W. *J. Am. Chem. Soc.* **2000**, *122*, 6175.
13. Trofimov, B.; Gusarova, N.; Brandsma, L. *Main Group Chem. News* **1996**, *4*, 18.
14. (a) Peterson, D. J. U.S. Patent 3,397,039, August 13, 1968; (b) Jarvis, R. F., Jr.; Jacubinas, R. M.; Kaner, R. B. *Inorg. Chem.* **2000**, *39*, 3243.
15. For the synthesis of (achiral) primary and secondary phosphines from alkylhalogenides and alkylphosphides, see: (a) Van Hooijdonk, M. C. J. M.; Gerritsen, G.; Brandsma, L. *Phosphorus, Sulfur Silicon* **2000**, *162*, 39; (b) Brandsma, L.; Gusarova, N. K.; Gusarov, A. V.; Ver-

kruijsse, H. D.; Trofimov, B. A. *Synth. Commun.* **1994**, *24*, 3219.

16. Compound **5** (selected data): colourless oil. ^{1}H NMR (CDCl$_3$) δ: 7.35–7.24 (m, 10H); 4.62 (dm, $J_{PH} = 371$ Hz, 1H); 4.51 (dd, $J = 5.9$, 11.8 Hz, 2H); 4.40 (dd, $J = 6.0$, 11.9 Hz, 2H); 3.66–3.51 (m, 4H); 2.42–2.30 (m, 2H); 1.21 (dd, $J = 7.3$, 14.9 Hz, 3H); 1.18 (dd, $J = 7.3$, 16.6 Hz, 3H); 0.91–0.00 (m, 3H). ^{13}C NMR (CDCl$_3$) δ: 137.89 (C); 137.81 (C); 128.40 (CH); 128.33 (CH); 127.75 (CH); 127.70 (CH); 127.66 (CH); 73.29 (CH$_2$); 73.19 (CH$_2$); 71.40 (d, $J = 2.3$ Hz, CH$_2$); 71.03 (d, $J = 2.3$ Hz, CH$_2$); 26.57 (d, $J = 33.6$ Hz, CH) 26.17 (d, $J = 33.6$ Hz, CH); 14.18 (d, $J = 2.3$ Hz, CH$_3$); 12.56 (d, $J = 1.5$ Hz, CH$_3$). ^{31}P NMR (CDCl$_3$) δ: 9.86 (m). MS (90 °C, 50 eV) m/z (rel%): 343 (8, M$^+$). HRMS for $C_{20}H_{29}BO_2P$: Calcd: 343.2002. Found: 343.1991. $[\alpha]_D^{20}$ -4.2 ± 0.09 (c 4.5, CHCl$_3$).
17. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons, 1999, p 79.
18. Compound **1** (selected data): colourless oil. ^{1}H NMR (CD$_3$OD) δ: 3.71 (ddd, $J = 4.7$, 8.5, 10.9 Hz, 3H); 3.44 (ddd, $J = 6.6$, 8.6, 10.8 Hz, 3H); 2.00 (m, 3H); 1.18 (dd, $J = 7.2$, 9.3 Hz, 9H). ^{13}C NMR (CD$_3$OD) δ: 67.39 (d, $J = 28.7$ Hz, CH$_2$); 30.85 (d, $J = 15.5$ Hz, CH); 14.56 (d, $J = 5.5$ Hz, CH$_3$). ^{31}P NMR (CD$_3$OD) δ: -6.73 (s).
19. RajanBabu, T. V.; Yan, Y.-Y.; Shin, S. *J. Am. Chem. Soc.* **2001**, *123*, 10207.
20. Christoffers, J.; Rößler, U. *Tetrahedron: Asymmetry* **1998**, *9*, 2349.
21. Hüttel, R.; Reinheimer, H.; Dietl, H. *Chem. Ber.* **1966**, *99*, 462.
22. In addition, a minor amount of a second species was detected with $m/z = 1054.2$, which is in agreement with an empirical formula $[\mathbf{1}_3Au_2Cl]^+Cl^-$.
23. Compound **12** (selected data): mp: 133–134 °C. UV/vis spectrum (CH$_3$OH), λ, nm (ε, M^{-1} cm^{-1}): 213 (sh) (12870), 249 (1305), 238 (2530). ^{1}H NMR (CD$_3$OD) δ: 3.93–3.78 (m, 6H); 2.66 (m, 3H); 1.37 (m, 9H). ^{13}C NMR (CD$_3$OD) δ: 66.00 (t, $J = 3.0$ Hz, CH$_2$); 33.25 (t, $J = 14.2$ Hz, CH); 14.85 (CH$_3$). ^{31}P NMR (CD$_3$OD) δ: 55.23 (s). MS (FD) m/z (rel%): 613.8 (100, $\mathbf{1}_2$Au$^+$). $[\alpha]_D^{20}$ +23.6 (c 0.93, MeOH). Crystal data for $[Au\{P(CHMeCH_2OH)_3\}_2]CF_3SO_3$ **12**: $C_{19}H_{42}AuF_3O_9P_2S$, $M_r = 762.49$, orthorhombic, space group $P2_12_12_1$, $a = 9.0690(4)$, $b = 14.1066(6)$, $c = 21.5358(9)$ Å, $V = 2755.1(2)$ Å^3, $F(000) = 1520$, D_c $(Z = 4) = 1.838$ g cm^{-3}, μ(Mo Kα) = 55.96 cm^{-1}, $2\theta_{max}$ 60°, wR (all data) 0.0408, conventional R (8102 data with $I > 2\sigma(I)$) 0.0184, Flack parameter $-0.012(3)$. Data collection was performed at 100(2) K on an X8 APEXII CCD diffractometer. The structure was solved by direct methods and refined by full-matrix least squares on F^2. CCDC 637239.
24. Assefa, Z.; Staples, R. J.; Fackler, J. P., Jr. *Acta Crystallogr., Sect. C* **1996**, *52*, 305.
25. Goodwin, N.; Henderson, W. *Polyhedron* **1998**, *17*, 4071.
26. Stefanescu, D. M.; Yuen, H. F.; Glueck, D. S.; Golen, J. A.; Zakharov, L. N.; Incarvito, C. D.; Rheingold, A. L. *Inorg. Chem.* **2003**, *42*, 8891.
27. Crystal data for **2·BH**$_3$ at 100 K: $C_9H_{24}BO_3P$, $M_r = 222.06$, orthorhombic, space group $P2_12_12_1$, $a = 6.7189(4)$, $b = 13.328(1)$, $c = 15.497(1)$ Å, $V = 1387.81(17)$ Å^3, $F(000) = 488$, D_c $(Z = 4) = 1.063$, μ(Mo Kα) = 1.82 cm^{-1}, $2\theta_{max}$ 60°, wR (all data) 0.1080, conventional R (2733 data with $I > 2\sigma(I)$) 0.0447, Flack parameter 0.05(15). Data collection was performed at 100(2) K on an X8 APEXII CCD diffractometer. The structure was solved by direct methods and refined by full-matrix least squares on F^2. Crystallographic data (excluding structure factors) for the structures in this Letter have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication Nos. CCDC 637239 and 642870 for **12** and **2·BH**$_3$, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].