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The Reaction of 2-Bromopyridine with a PH_3/H_2 System in the KOH/DMSO Suspension: A Short Route to Tris(2-pyridyl)phosphine

Boris A. Trofimov, Nina K. Gusarova, Alexander V. Artem'ev, Svetlana F. Malysheva, Nataliya A. Belogorlova, and Anastasiya O. Korocheva

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russian Federation

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ABSTRACT: *The straightforward reaction of 2-bromopyridine with a PH_3/H_2 system (generated from phosphorus red and aqueous alkali) in the superbasic KOH/DMSO/(H_2O) suspension under mild conditions (70°C, 1.5 h, atmospheric pressure) affords selectively and cleanly tris(2-pyridyl)phosphine in 50% yield; no admixtures of the expected primary and secondary pyridylphosphines were observed in the crude product.*
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INTRODUCTION

Pyridylphosphines are widely used for the synthesis of transition metal organic compounds [1] with unusual coordination properties and catalytic activity [2]. The affinity of such ligands toward catalytically active transition metals makes them ideal tools for constructing heteroatomic architectures [3]. Tris(pyridyl)phosphines were shown to be rewarding building blocks for the diverse supramolecular structures [4]. Besides, they were reported to be intermediates for syntheses of heteroatom and inorganic compounds [5] and medicine precursors [6]. Among pyridylphosphines, (2-pyridyl)phosphines, in particular, tertiary tris(2-pyridyl)phosphine, are of special interest due to the geminal disposition of such chemically and biologically important donor heteroatoms as nitrogen and phosphorus [7], which secures the cooperative chelating interaction with different electron-deficient substrates [3]. Diverse ligations of tris(2-pyridyl)phosphine led to numerous novel and useful complexes [3,8], some of which were explored as catalysts for such industrially meaningful reactions as methoxycarbonylation of alkynes [9], hydroformylation of alkenes [10], ethylene polymerization [11], and Diels–Alder synthesis [12].

Pyridylphosphines are usually synthesized from pyridyl metal derivatives (Li, Mg) and phosphorus halides [3]. These syntheses require low temperature (−110°C for lithium derivatives [13]) and inert atmosphere to avoid isomerization and deterioration of intermediates. For the isolation of the products (yields about 45%), laborious column chromatography procedures are necessary [13]. Recently [14], tris(2-pyridyl)- and tris(3-pyridyl)phosphines were prepared in 70–75% yields via the Grignard route (dry THF, −78°C). In the latter case, the target phosphines were isolated by tedious extraction of the resulting solid with a large amount of diethylamine, because the Mg^{2+} cations strongly increased the solubility of these phosphines in aqueous media [14].

Correspondence to: B. A. Trofimov; e-mail: boris_trofimov@irioch.irk.ru.
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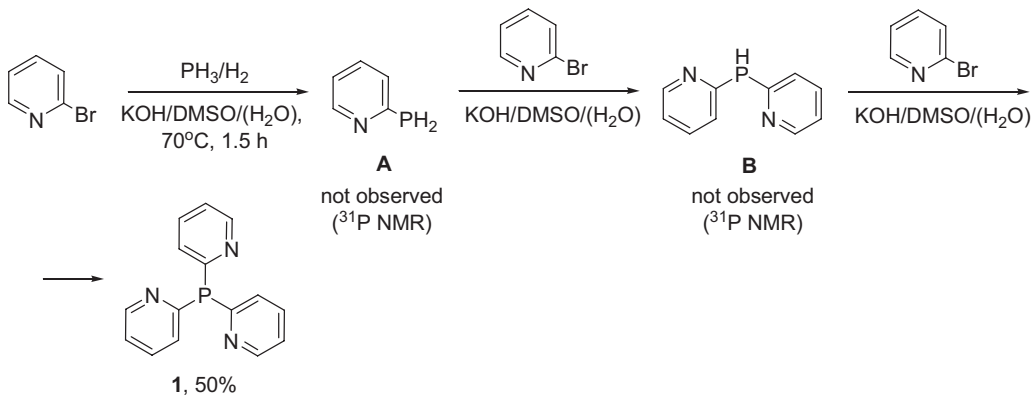
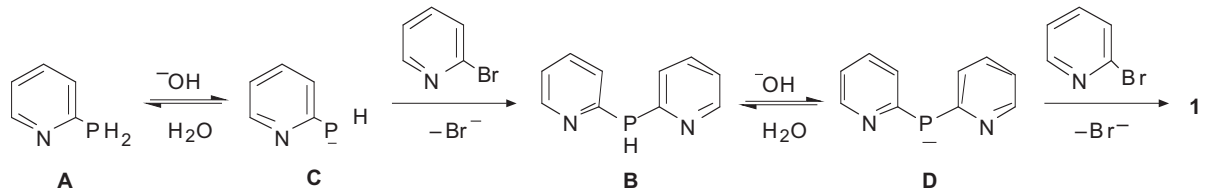


SCHEME 1 Synthesis of tris(2-pyridyl)phosphine from 2-bromopyridine and phosphine.



SCHEME 2 Plausible mechanism of 2-bromopyridine phosphination.

RESULTS AND DISCUSSION

In this article, we describe for the first time a new simple and efficient synthesis of tris(2-pyridyl)phosphine by the straightforward reaction of 2-bromopyridine with a PH_3/H_2 mixture. The process proceeds smoothly under mild conditions (70°C, atmospheric pressure), when the PH_3/H_2 mixture (~1:1) is passed through (45–50 bubbles per min) the superbasic suspension KOH/DMSO/(H_2O), 2-bromopyridine gradually (1.5 h) being dropped to the reaction medium (Scheme 1). The yield (not optimized) of tris(2-pyridyl)phosphine (**1**) is 50%. The PH_3/H_2 reagent is readily generated at the controlled rate by slow addition of aqueous KOH (50%) to the phosphorus red/toluene suspension at 75–80°C according to the protocol [15]. Here, the hydrogen gas is likely to protect (against oxidation) the P(III) species in the reaction process. The synthesis is fairly selective and clean: Only tris(2-pyridyl)phosphine is formed, and no admixtures of the expected primary (**A**) and secondary (**B**) phosphines as well as any position isomers are observed in the reaction mixture (Scheme 1).

Indeed, our failure to detect (^{31}P NMR) intermediates **A** and **B** in the resulting crude product seems surprising, because every next step toward the synthesis of final tris(2-pyridyl)phosphine should be more sterically hindered as the formal aromatic substitution of the bromine atom in the 2-bromopyridine ring with participation of all bulkier phosphide-anions **C** and **D** (ionized phosphines **A** and **B**) (Scheme 2).

Moreover, the repulsive interaction between phosphorus-centered anions **C**, **D**, and nitrogen lone electron pairs should additionally interfere with the direct nucleophilic substitution. Apparently, all these negative effects are excessively compensated by the higher concentration of the intermediate anions **C** and **D**. The latter is an expected result of the augmented acidity of phosphines **A** and **B**.

An alternative to this mechanism may be the elimination–addition scheme (via dehydropyridine), although the 100% regioselectivity of the reaction seems to be not in keeping with this assumption. Another alternative could involve the nucleophilic substitution of bromine by hydroxide anion and a further reaction of the 2-hyrdoxypyridine 2-pyridone mixture with phosphines. However, these special mechanistic issues are the subject of our further investigation.

CONCLUSION

In conclusion, a one-pot synthesis of tris(2-pyridyl)phosphine in 50% yield by the straightforward reaction of available 2-bromopyridine with the

PH_3/H_2 system in the superbasic KOH/DMSO/(H_2O) suspension under mild conditions (70°C, 1.5 h, atmospheric pressure) has been developed. The controlled PH_3/H_2 gas flow has been safely generated by dosed addition of aqueous KOH to red phosphorus in toluene. An advantageous feature of the synthesis is its high selectivity: No corresponding primary and secondary phosphines as well as their position isomers have been detected in the crude reaction mixture. This new simple access to tris(2-pyridyl)phosphine substantially expands its application as a powerful tripodal ligand for design of metal complex catalysts and novel heteroatomic supramolecular architectures, potent synthetic building block, and drug precursor.

EXPERIMENTAL

The microanalyses were performed on a Flash EA 1112 Series elemental analyzer. The Fourier transform IR spectrum was run on a Bruker Vertex 70 instrument. The ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AV-400 spectrometer (400.13, 100.61, and 161.98 MHz, respectively) and referenced to H_3PO_4 (^{31}P NMR) as an external standard. Chemical shifts (δ) are expressed in ppm downfield from hexamethyldisiloxane (0.05 ppm for a ^1H NMR scale) as an internal standard. The PH_3/H_2 mixture was prepared from red phosphorus, KOH, and H_2O according to the protocol [15]. Red phosphorus, 2-bromopyridine, potassium hydroxide (~15% water content), and DMSO (1% water content) were employed as commercial products.

Safety Note: Phosphine and its derivatives are toxic! These materials should be handled with great caution.

*Tris(2-pyridyl)phosphine (**1**)*

To a suspension of $KOH{\cdot}0.5H_2O$ (20.0 g, 307.2 mmol), DMSO (50.0 mL), and water (12.0 mL), blown with argon and saturated with the PH_3/H_2 mixture, a solution of 2-bromopyridine (10.0 g, 63.3 mmol) in DMSO (10 mL) was added dropwise for 1.5 h at 70°C under stirring and continuous passing of the PH_3/H_2 mixture at a rate of 45–50 bubbles per min. Then the PH_3/H_2 gas feeding was stopped. The mixture was cooled, diluted with water (100 mL), and extracted with chloroform (3 × 30 mL). The extract was washed with water (3 × 30 mL) and dried over K_2CO_3. The solvent was removed under reduced pressure, and the residue was washed with cold *i*−PrOH (1 × 5 mL) and dried in vacuo (1 Torr) to give pure phosphine **1** as microcrystalline powder. Yield: 2.8 g (50%), mp 115–116°C (*i*-PrOH), lit. 113°C [13]. IR (KBr): 3039, 2961, 2900, 1572, 1558, 1450, 1424, 1413, 1283, 1276, 1147, 1085, 1045, 987, 960, 907, 896, 774, 765, 743, 721, 712, 618, 548, 513, 503, 496, 426, 407, 395 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.18–7.23 (m, 3H, H-5), 7.41 (d, $^3J_{HH}$ = 7.0 Hz, 3H, H-3), 7.58–7.64 (m, 3H, H-4), 8.72 (d, $^3J_{HH}$ = 3.70 Hz, H-6). ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 122.5 (C-5), 128.9 (d, $^1J_{CP}$ = 19.3 Hz, C-2), 135.6 (d, $^3J_{CP}$ = 2.6 Hz, C-4), 150.1 (d, $^2J_{CP}$ = 19.3 Hz, C-3), 161.5 (C-6). ^{31}P NMR (161.98 MHz, $CDCl_3$): δ = −0.06. Anal. Calcd for $C_{15}H_{12}N_3P$: C, 67.92; H, 4.56; N, 15.84; p, 11.68. Found: C, 67.85; H, 4.41; N, 15.74; p, 11.50.

REFERENCES

[1] For recent select examples, see: (a) Barton, B. E.; Rauchfuss, T. B. J Am Chem Soc 2010, 132, 14877–14885; (b) Liu, J.; Jacob, C.; Sheridan, K. J.; Al-Mosule, F.; Heaton, B. T.; Iggo, J. A.; Matthews, M.; Pelletier, J.; Whyman, R.; Bickley, J. F.; Steiner A. Dalton Trans 2010, 39, 7921–7935; (c) West, N. M.; Labinger, J. A.; Bercaw, J. E.; Organometallics 2011, 30, 2690–2700; (d) Antelo, J. M.; Adrio, L.; Pereira, M. T.; Ortigueira, J. M.; Fernandez, A.; Vila, J. M. Eur J Inorg Chem 2011, 11069–11076.

[2] For recent select examples, see: (a) Tang, C.-M.; Zeng, Y.; Yang, X.-G.; Lei, Y.-C.; Wang, G.-Y. J Mol Catal, A: Chem 2009, 314, 15–20; (b) Kumar, P.; Kumar Singh, A.; Sharma, S.; Shankar Pandey, D. J Organomet Chem 2009, 694, 3643–3652; (c) Muranaka, M.; Hyodo, I.; Okumura, W.; Oshiki, T. Catal Today 2011, 164, 552–555.

[3] For reviews, see: (a) Newkome, G. R. Chem Rev 1993, 93, 2067–2089; (b) Zhang, Z. Z.; Cheng, H. Coord Chem Rev 1996, 147, 1–39; (c) Espinet, P.; Soulantica, K. Coord Chem Rev 1999, 193–195, 499–566; (d) Sadimenko, A. P. Adv Heterocycl Chem 2011, 104, 391–475.

[4] (a) Slagt, V. F.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. J Am Chem Soc 2004, 126, 1526–1536; (b) Kleij, A. W.; Kuil, M.; Tooke, D. M.; Spek, A. L.; Reek, J. N. H. Inorg Chem 2005, 44, 7696–7698.

[5] For example, see: (a) Gros, P.; Younes-Millot, C. B.; Fort, Y, Tetrahedron Lett 2000, 41, 303–306; (b) Alcarazo, M.; Suarez, R. M.; Goddard, R.; Fuerstner, A. Chem Eur J 2010, 16, 9746–9749; (c) Kharat, A. N.; Bakhoda, A.; Hajiashrafi, T.; Abbasi, A. Phosphorus, Sulfur Silicon Relat Elem 2010, 185, 2341–2347.

[6] (a) Berners-Price, S. J.; Bowen, R. J.; Galettis, P.; Healy, P. C.; McKeage, M. J Coord Chem Rev 1999, 185–186, 823–836; (b) Roman Luque-Ortega, J.; Reuther, P.; Rivas, L.; Dardonville, C. J Med Chem 2010, 53, 1788–1798; (c) Kharat, A. N.; Bakhoda, A.; Foroutannejad, S.; Foroutannejad, C. Z Anorg Allg Chem 2011, 637, 1–6.

[7] Szczepura, L. F.; Witham, L. M.; Takeuchi, K. J Coord Chem Rev 1998, 174, 5–32.
[8] For recent select examples, see: (a) Saucedo Anaya, S. A.; Hagenbach, A.; Abram, U. Polyhedron 2008, 27, 3587–3592; (b) Adeyemi, O. G.; Liu, L.-K. Inorg Chim Acta 2009, 362, 477–482; (c) Woollard-Shore, J. G.; Holland, J. P.; Jones, M. W.; Dilworth, J. R. Dalton Trans 2010, 39, 1576–1585; (d) Bakhoda, A.; Safari, N.; Amani, V.; Khavasi, H. R.; Gheidi, M. Polyhedron 2011, 30, 2950–2956.
[9] Drent, E.; Arnoldy, P.; Budzelaar, P. H. M. J Organomet Chem 1994, 475, 57–63 and 247–253.
[10] Kurtev, K.; Ribola, D.; Jones, R. A.; Cole-Hamilton, D. J.; Wilkinson, G. J Chem Soc, Dalton Trans 1980, 55–58.
[11] Karam, A.; Tenia, R.; Martinez, M.; López-Linares, F.; Albano, C.; Diaz-Barrios, A.; Sánchez, Y.; Catarí, E.; Casas, E.; Pekerar, S.; Albornoz, A. J Mol Catal, A: Chem 2007, 265, 127–132.
[12] Kuo, C.-Y.; Fuh, Y.-S.; Shiue, J.-Y.; Yu, S. J.; Lee, G.-H.; Peng S.-M. J Organomet Chem 1999, 588, 260–267.
[13] Bowen, R. J.; Garner, A. C.; Berners-Price, S. J.; Jenkins, I. D.; Sue, R. E. J Organomet Chem 1998, 554, 181–184.
[14] Kluwer, A. M.; Ahmad, I.; Reek, J. N. H. Tetrahedron Lett 2007, 48, 2999–3001.
[15] Gusarova, N. K.; Malysheva, S. F.; Kuimov, V. A.; Belogorlova, N. A.; Mikhailenko, V. L.; Trofimov, B. A. Mendeleev Commun 2008, 18, 260.