Convenient Preparation of Tri-*tert***-butylphosphonium Tetrafluoroborate**

Tanguy Saget,^{a,b} Nicolai Cramer*a

 Laboratory of Asymmetric Catalysis and Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSA, BCH 4305, 1015 Lausanne, Switzerland Fax +41(21)6939700; E-mail: nicolai.cramer@epfl.ch

^b Laboratorium für Organische Chemie, ETH Zürich, HCI H 304, Wolfgang-Pauli-Strasse 10, 8093 Zurich, Switzerland

Received 28 April 2011; revised 25 May 2011



Abstract: The versatile tri-*tert*-butylphosphonium tetrafluoroborate ligand is prepared in a convenient, simple, and high-yielding procedure without the isolation of sensitive intermediates.

Key words: ligands, homogeneous catalysis, phosphorus, transition metals, Grignard reaction



Scheme 1 Synthesis of tri-*tert*-butylphosphonium tetrafluoroborate from inexpensive starting materials without isolation and purification of pyrophoric material

The introduction of basic and bulky trialkylphosphines, such as tricyclohexylphosphine and tri-tert-butylphosphine, has had a tremendous impact in transition-metal catalysis.¹ According to the carbonyl stretching frequency of the $Ni(CO)_3[P(t-Bu)_3]$ complex, tri-*tert*-butylphosphine is a very strong electron-donating ligand.² It is also a sterically very bulky ligand having a large cone angle of 182°.³ Its electron-rich nature facilitates the oxidative addition of previously reluctant substrates (e.g., aryl chlorides) in palladium-catalyzed reactions even at ambient temperature.⁴ The steric demand of the phosphine aids the formation of coordinatively unsaturated species of crucial importance for initiating catalytic processes and its steric bulk enhances the rate of reductive elimination.⁵ Therefore, tritert-butylphosphine has found widespread application in many transition-metal-catalyzed reactions (Scheme 2).



Scheme 2 Illustrating the versatility of tri-*tert*-butylphosphonium tetrafluoroborate in palladium catalysis; the oxidative addition of aryl chlorides enables a myriad of reactions

SYNTHESIS 2011, No. 15, pp 2369–2371 Advanced online publication: 14.07.2011 DOI: 10.1055/s-0030-1260113; Art ID: Z44711SS © Georg Thieme Verlag Stuttgart · New York However, tri-tert-butylphosphine has a low melting point (30 °C), pyrophoric nature, and high oxidation propensity in the solid state as well as in solution, hence it requires careful handling and sophisticated inert gas techniques. A broadly applicable solution to these shortcomings was made by Fu and co-workers, who introduced trialkylphosphonium salts as replacements for the free phosphines.⁶ In stark contrast, these salts are nonhygroscopic, they have high melting points, and, most importantly, they are indefinitively air-stable compounds. The free phosphine (pK_{a}) $(11.4)^7$ is subsequently generated conveniently in situ by treatment with almost any base, which is usually required in stoichiometric amounts, in the individual transitionmetal-catalyzed process. Although widely available, tri*tert*-butylphosphonium tetrafluoroborate (1) has a relatively high price.⁸ The reported synthesis of the phosphonium salt requires the hazardous and equally expensive free phosphine as a reactant. In contrast to triarylphosphines, sterically demanding trialkylphosphines are problematic to synthesize from phosphorus trichloride and magnesium or lithium organyls. Poor yields and formation of dialkylchlorophosphines are often observed. The addition of copper salts has largely addressed this issue and good yields can be obtained.9 Several dialkyl(aryl)phosphonium salts can be directly isolated by precipitation from the crude reaction mixture by addition of aqueous acids such as tetrafluoroboric acid.¹⁰ However, the most versatile tri-tert-butylphosphonium salts are not accessible by this method as they possess a relatively high solubility in water. Hence, their preparation requires a tedious isolation and purification procedure of the highly oxidation-sensitive and pyrophoric free phosphine.

Herein we report a procedure addressing these shortcomings and present a synthesis of tri-tert-butylphosphonium tetrafluoroborate (1) from inexpensive starting materials without the need for sophisticated equipment that gives 1 reliably, in good yields, and on a 50-mmol scale (Scheme 1). Simple extraction procedures followed by crystallization avoid any handling of air sensitive and hazardous phosphine. We use advantageously the high solubility of the tri-tert-butylphosphonium salts in aqueous solution, thus allowing the removal of uncharged and apolar byproducts by extraction with hydrocarbon or ethereal solvents. The desired phosphonium salt itself is subsequently extracted with dichloromethane. By such treatment, the obtained crude product already has of a purity of >95% (1 H NMR). The main contamination consists of di-tert-butylphosphonium tetrafluoroborate. A single recrystallization from ethanol reduces this impurity to less than 0.3% and provides 1 as crystalline material. This also allows the previously unobtained X-ray crystallographic structure of the phosphonium tetrafluoroborate to be recorded (Figure 1).11



Figure 1 ORTEP representation of tri-*tert*-butylphosphonium tetrafluoroborate (probability ellipsoids at 50%, hydrogen atoms omitted for clarity)

In summary, we have developed an experimentally simple and practical protocol for the synthesis tri-*tert*-butylphosphonium tetrafluoroborate. This procedure gives good yields and high purities in a scalable fashion and requires only basic equipment and inexpensive chemicals.

Hexane was dried by passage over activated alumina under an N₂ atmosphere prior to use. Technical grade hexane and CH₂Cl₂ were used for the workup. CuBr·Me₂S (Acros), LiBr (Fluka), PCl₃ (Fluka), 2.0 M *t*-BuMgCl in Et₂O (TCI) were used as received. 48% aq HBF₄ was purchased from Acros and diluted to 3 M prior to use. The soln was briefly degassed prior to use with three vacuum cycles [300 mbar/N₂]. The melting point was obtained on a Büchi B-540 apparatus in open capillary tubes. ¹H NMR data were acquired on a DPX-400 400 MHz spectrometer in CDCl₃ with TMS as reference. ¹³C NMR data were acquired with ¹H-decoupling on a Bruker DPX-400 100 MHz spectrometer in CDCl₃, relative to the triplet at δ = 77.0 ppm for CDCl₃. IR data were recorded on a Bruker ALPHA FT-IR spectrophotometer. Combustion elemental analyses was performed by the analytical facilities of EPFL.

Tri-tert-butylphosphonium Tetrafluoroborate (1)

To a dried 500-mL three-neck flask equipped with an addition funnel, an internal thermometer, and a magnetic stirrer bar were added CuBr·Me₂S (514 mg, 2.50 mmol) and LiBr (434 mg, 5.00 mmol). The reaction vessel was purged with N₂ and hexane (100 mL) was added. PCl₃ (4.37 mL, 50.0 mmol) was added to the suspension and the reaction was cooled with an ice bath. 2.0 M t-BuMgCl in Et₂O (100 mL, 200 mmol) was added dropwise and during the addition of the first 50 mL, the internal temperature was kept below 8 °C. The flask was warmed with an ambient water bath and the remainder of the t-BuMgCl soln was added and the mixture was stirred vigorously for 13 h at 23 °C. The mixture was then recooled with an ice bath and 3 M aq HBF₄ soln (175 mL, 525 mmol) was carefully added, keeping the internal temperature below 25 °C. The biphasic mixture was stirred for 15 min and filtered over a pad of Celite. The layers were separated and the aqueous layer was washed with hexane $(2 \times 100 \text{ mL})$ to remove apolar impurities. The aqueous layer was then extracted with CH_2Cl_2 (3 × 200 mL). The combined CH₂Cl₂ layers were dried (MgSO₄), filtered, and evaporated in vacuo to afford crude tri-tert-butylphosphonium tetrafluoroborate (12.0 g) as a white solid (96% NMR purity). Crystallization (EtOH, 6 mL/g) afforded analytically pure material (9.76 g) as colorless plates. The mother liquor was concentrated and crystallization (EtOH) afforded additional product (1.06 g) (75% combined yield); mp 300-302 °C (dec.) (EtOH).

IR (ATR): 3003, 1474, 1382, 1179, 1052, 1029, 907, 885, 726 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 6.08 (d, ¹*J*_{PH} = 465 Hz, 1 H), 1.67 (d, ³*J*_{PH} = 15.3 Hz, 27 H).

¹³C NMR (100 MHz, CDCl₃): δ = 37.1 (d, ¹*J*_{PC} = 28.8 Hz), 30.1.

³¹P NMR (162 MHz, CDCl₃): δ = 51.5.

Anal. Calcd for $C_{12}H_{28}BF_4P$: C, 49.68; H, 9.73. Found: C, 49.68; H, 9.63.

Acknowledgment

We thank the ETH Zurich (ETH-16 09-3) as well as Prof. E. M. Carreira for generous support. The Fonds der Chemischen Industrie is acknowledged for a Liebig-Fellowship to N.C. We thank Dr. R. Scopelliti (EPFL) for the X-ray crystallographic analysis of **1**.

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- (11) Crystallographic data for tri-*tert*-butylphosphonium tetrafluoroborate C₁₂H₂₈BF₄P, *M* = 290.13, monoclinic, space group *P*21/*c*, *a* = 12.3185(17) Å, *b* = 23.883(4) Å, *c* = 16.219(3) Å, β = 90.319(13), *V* = 4771.6(13) Å³, *Z* = 12, *D*_{calc} = 1.212 mg m⁻³, *T* = 100 K, reflections collected:

26253, independent reflections: 6289, R(all) = 0.1017, wR(gt) = 0.3027. CCDC 822956 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.