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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

PREPARATION OF (*S,S*)-1,2-BIS(*tert*-BUTYLMETHYLPHOSPHINO)ETHANE ((*S,S*)-*t*-Bu-BISP*) AS A RHODIUM COMPLEX
[Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene] (S,S)-1,2-bis(*M*, -butymethylphosphino)ethane, trafluoroborate(1-)]
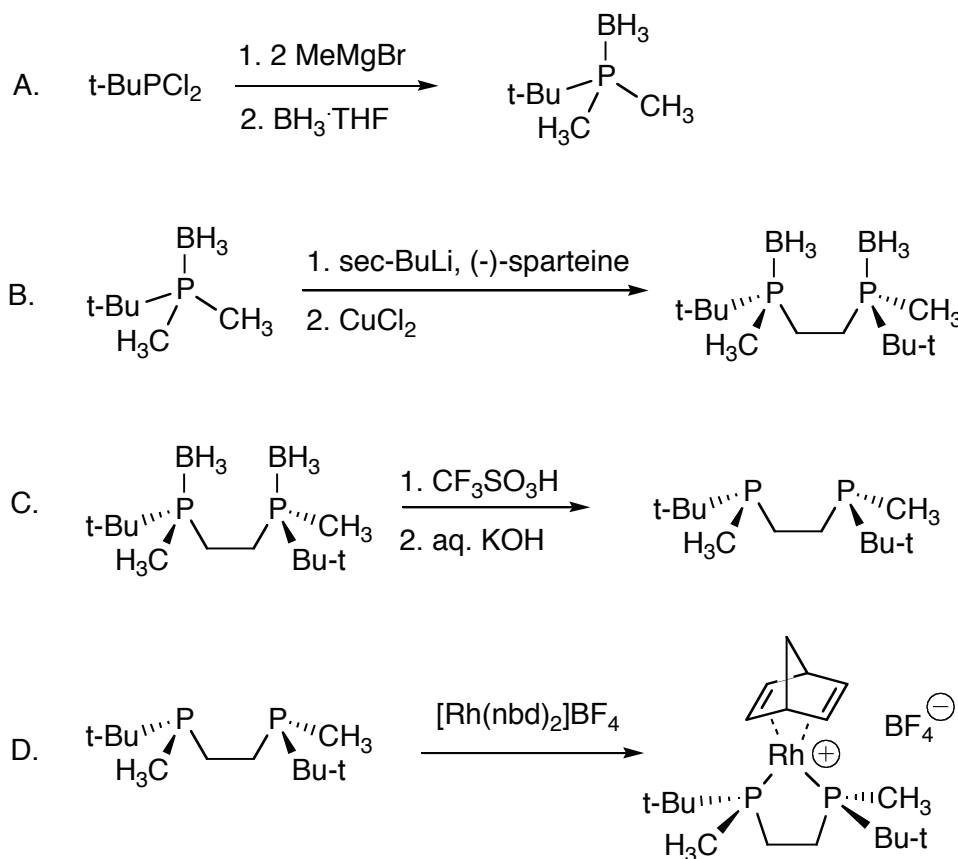
Submitted by Karen V. L. Crépy and Tsuneo Imamoto.[1]
Checked and substantially modified by Günter Seidel and Alois Fürstner.

1. Procedure

Caution! All reactions must be carried out in a well-ventilated hood.

A. tert-Butyl(dimethyl)phosphine–Borane. A 500-mL, three-necked flask equipped with a large football-shaped magnetic stirring bar, a thermometer, a three-way tap connected to an argon line, and a 250-mL pressure-equalizing dropping funnel fitted with a glass stopper is flame dried under vacuum and purged with argon (Note 1). The flask is charged with *tert*-butyldichlorophosphine (12.18 g, 77 mmol) (Note 2) and THF (120 mL) (Note 3) under argon and the resulting solution is cooled to −10 °C using a

cryostat. A solution of methylmagnesium bromide (3.0 M in Et$_2$O, 57 mL, 171 mmol) (Note 4) diluted with THF (100 mL) is added dropwise over 0.5 h at such a rate as to maintain the internal temperature below 0 °C, and the resulting heterogeneous mixture is stirred for 5 h at room temperature. A solution of borane–THF complex (1.0 M in THF, 93 mL, 93 mmol) (Note 5) is then added dropwise over 20 min at –10 °C and stirring is continued at room temperature overnight (18 h). The mixture is cautiously poured into ice/water (120 mL) containing concentrated HCl (30 mL) (Note 6) and the resulting solution is vigorously stirred for 15 min. The layers are separated, the aqueous phase is extracted with ethyl acetate (2 x 100 mL), the combined organic layers are washed with brine (150 mL), dried over Na$_2$SO$_4$, filtered and evaporated under reduced pressure. The residue is recrystallized from hot hexane (40 mL) and dried under vacuum to give the *tert*-butyl(dimethyl)phosphine–borane adduct as a white solid (6.1 g, 61 %) (Notes 7,8).

B. (S,S)-1,2-Bis(boranato(tert-butyl)methylphosphino)ethane. A 500-mL, three-necked flask equipped with a football-shaped magnetic stirring bar, a thermometer, a three-way tap connected to an argon line, and a 100-mL pressure-equilizing dropping funnel fitted with a glass stopper is flame-dried under vacuum and filled with argon. After cooling to ambient temperature, the flask is charged with (–)-sparteine (8.18 g, 35 mmol) and diethyl ether (40 mL) (Note 3) and the resulting solution is cooled to –78 °C using a cryostat. *sec*-Butyllithium (1.3 M in cyclohexane, 26.8 mL, 35 mmol) is added dropwise at that temperature over 5 min and stirring is continued for 30 min before a solution of the *tert*-butyl(dimethyl)phosphine–borane adduct (4.21 g, 31.9 mmol) in diethyl ether (40 mL) is added dropwise over 30 min. The mixture is stirred at –78 °C for 1 h and –50 °C for 4 h. Copper(II) chloride (5.6 g, 41 mmol) (Note 9) is added with vigorous stirring and the resulting mixture is gradually warmed to room temperature overnight. Aqueous ammonia (25-28%, 40 mL) is added, the layers are separated, the bright blue aqueous phase is extracted with ethyl acetate (2 x 50 mL), the combined organic layers are successively washed with water (30 mL), aqueous HCl (3 M, 2 x 30 mL), water (30 mL), and brine (30 mL) before being dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The residue is recrystallized twice from toluene at 80 °C (20 mL each) (Note 10) to afford diastereomerically pure (*S,S*)-1,2-bis(boranato(*tert*-butyl)methylphosphino)ethane (2.0 g, 48 %) as

white needles (Note 11). The enantiomeric purity is checked by HPLC analysis using a chiral column (Note 12).

C. *(S,S)-1,2-Bis-((tert-butyl)methylphosphino)ethane ((S,S)-t-Bu-BisP*))*. A 100-mL, two-necked flask equipped with a magnetic stirring bar, a three-way tap connected to an argon line, and a glass stopper is flame-dried under vacuum and filled with argon after reaching ambient temperature. The flask is charged with (*S,S*)-1,2-bis(boranato(*tert*-butyl)methylphosphino)ethane (1.14 g, 4.4 mmol) and toluene (35 mL) (Note 3) and the resulting mixture is cooled to 0 °C. Trifluoro-methanesulfonic acid (1.92 mL, 22 mmol) is added dropwise and the mixture is stirred for 15 min at 0 °C and for 45 min at ambient temperature. The solvent is evaporated under reduced pressure before a solution of potassium hydroxide (2.44 g, 43 mmol) in freshly degassed ethanol/water (9:1 ratio, 15 mL) (Note 13) is added, and the resulting mixture is stirred at 50 °C for 2 h under argon. After reaching ambient temperature, the mixture is extracted four times with diethyl ether (20 mL each) while keeping the positive pressure of argon. The combined organic phases are dried over Na_2SO_4 and passed through a short column of basic alumina (80 g) under argon (Note 14). The column is carefully rinsed with degassed diethyl ether (total volume 180 mL) and the combined eluents are evaporated to give a colorless pasty oil which solidifies on cooling to 0 °C (980 mg, 95%). The free diphosphine is immediately subjected to complexation with a transition metal precursor.

D. *[Rh((S,S)-t-Bu-BisP*))(nbd)]BF₄*. A 250-mL, two-necked flask equipped with a magnetic stirring bar, a glass stopper, and a three-way tap connected to an argon line is flame-dried under vacuum and filled with argon. After reaching ambient temperature, the flask is charged with [Rh(nbd)₂]BF₄ (1.17 g, 3.1 mmol) (Note 15) and THF (100 mL). A solution of (*S,S*)-1,2-bis-((*tert*-butyl)methylphosphino)ethane (0.77 g, 3.3 mmol) in THF (40 mL) is added via syringe to this suspension and stirring is continued for 2 h leading to the formation of an almost clear solution. This mixture is filtered under argon and the filtrate is evaporated. The orange powder is dissolved in hot THF until a clear solution is formed. This solution is slowly cooled to 0 °C, leading to the precipitation of red cubes that are removed through filtration under argon. The filtrate is evaporated and the residue is recrystallized again by the same procedure. The combined crops of five recrystallizations are dried under vacuum to give the rhodium complex in analytically pure form (687 mg, 43 %) (Notes 16, 17).

2. Notes

1. Argon (> 99.999%) was used by the checkers.

2. *tert*-Butyldichlorophosphine was purchased from Aldrich and used as received. *tert*-Butyldichlorophosphine is moderately air-sensitive and must be handled under argon.

3. THF, Et$_2$O, and toluene were freshly distilled from sodium/ benzophenone at atmospheric pressure under argon immediately prior to use.

4. The submitters used methylmagnesium bromide in THF (1.0 M in THF) purchased from the Tokyo Kasei Company. The checkers purchased methylmagnesium bromide (3 M in Et$_2$O) from Aldrich. It was transferred from the commercial bottle to the dropping funnel under argon *via* cannula.

5. Borane-THF complex was purchased from Kanto Chemical Company. The checkers purchased this reagent from Aldrich. Borane-THF is air-sensitive and must be handled under argon.

6. *CAUTION*: Excess methylmagnesium bromide and borane–THF complex react violently with water while liberating a large amount of gas. Slow addition under stirring is necessary. The use of a large Erlenmeyer flask is recommended.

7. The submitters reported a yield of 77-81% (19.2-20.4 g scale). The *tert*-butyl(dimethyl)phosphine–borane adduct prepared by this procedure shows the following physical and spectroscopic data: mp 164-165 °C (hexane); R$_f$ 0.44 (5:1 hexane/ethyl acetate); ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.23 [d, 6H, ^2J(P,H) = 9.9 Hz], 1.16 [d, 9H, ^3J (P,H) = 14 Hz], 0.44 [dq, 3H, J(B,H) = 95 Hz, ^2J (P,H) = 15 Hz]; ^{13}C NMR (100 MHz, CDCl$_3$): δ 26.6 [d, J(P,C) = 35 Hz], 24.7 [d, ^2J (P,C) = 2.2 Hz], 7.3 [d, J(P,C) = 35.6 Hz]; ^{11}B NMR (96 MHz, CDCl$_3$): δ −39.9 [dq, J(B,H) = 95 Hz, J(P,B) = 63 Hz]; ^{31}P NMR (121 MHz, CDCl$_3$): δ 20.9 [q, J(P,B) = 62 Hz]. IR (KBr): 2970, 2370, 1070, 945, 920 cm^{-1}.

8. The malodorous smell of the reaction/work-up glassware is removed by immersing all vessels for 1 h in a mixture of domestic bleach and water (ca 1/10 ratio).

9. Finely powdered copper(II) chloride was dried for 2 h at 130–140 °C under vacuum prior to use.

10. The submitters report that 4-5 recrystallizations were necessary to obtain the desired (*S,S*)-t-Bu-BisP*–borane complex in pure form. It is

important that the solid is carefully dried before proceeding to the next recrystallization.

11. The submitters reported yields of 60% (2.15 g scale) and 51-55% (5.3-5.6 g scale).

12. (*S,S*)-1,2-bis(boranato(*tert*-butyl)methylphosphino)ethane shows the following analytical and spectroscopic data: mp = 186-187.5 °C; the submitters report a mp = 182-184 °C. R_f 0.22 (5:1 hexane/ethyl acetate); $[\alpha]^{28}_D$ –9.1 (c 1.21, chloroform); ee = 99.1% (250 mm Chiralcel OD-H, 0.5 mL/min; n-heptane/i-propanol = 9:1; RI detection; t = 15.3 min); IR (KBr): 2960, 2380, 2350, 1185, 1065, 765 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.99 (m, 2H), 1.60 (m, 2H), 1.21 [d, 6H, ^2J(P,H) = 10 Hz], 1.17 [d, 18 H, ^3J(P,H) = 14 Hz], 0.38 [q, 6H, J(B,H) = 95 Hz]; ^{11}B NMR (128 MHz, CDCl$_3$): δ –41.1 [dq, J(P,B) = 63 Hz, J(B,H) = 94 Hz]; ^{13}C NMR (100 MHz, CDCl$_3$): δ 27.7 [d, J(P,C) = 34 Hz], 25.1, 15.9 [d, J(P,C) = 30 Hz], 5.6 [d, J(P,C) = 34 Hz]; ^{31}P-NMR (162 MHz, CDCl$_3$): δ 30.1. MS (EI) *m/z* (rel. intensity): 262 ([M$^+$], 4), 261 (25), 260 (15), 259 (27), 258 (15), 257 (20), 256 (9), 247 (100), 203 (24), 191 (21), 189 (55), 133 (17), 108 (5), 93 (6), 75 (5), 57 (42), 41 (41), 29 (17); HR-MS (ESIpos, [M$^+$ + NH$_4$]): calcd. 280.26656, found 280.26674.

13. The checkers prepared the degassed solvents by two freeze/thaw cycles, whereas the submitters recommended the following procedure: The solvent is introduced in a two-necked flask fitted with a septum and a three-way tap connected to an argon balloon. It is placed in an ultra-sound bath and vacuum/argon cycles are applied three times.

14. Free phosphines are usually air-sensitive compounds and must be handled under argon. Therefore, all flasks must be evacuated and purged with argon three times before introducing any free phoshines. The alumina column must also be the subject of the same treatment (a thin pressure-equalizing dropping funnel is best used).

15. The checkers prepared the complex [Rh(nbd)$_2$]BF$_4$ in the following way: AgBF$_4$ (931 mg, 4.8 mmol) is added to a solution of [Rh(nbd)Cl]$_2$ (1.001 g, 2.17 mmol) and norbornadiene (1.8 mL, 16 mmol) in CH$_2$Cl$_2$ (30 mL) and the resulting mixture is stirred at ambient temperature for 4 h under argon. The precipitate is filtered through a pad of Celite, the filtrate is evaporated, and the residue is triturated with Et$_2$O (50 mL). The solid material formed is filtered, rinsed with Et$_2$O (5 mL) and dried in vacuum to give [Rh(nbd)$_2$]BF$_4$ as a dark red, air sensitive, crystalline solid.

Anal. calcd. for $C_{14}H_{16}RhBF_4$ (373.99): C 44.96, H 4.31; found: C 45.09, H 4.35.

16.   The submitters report a yield of 62% (2.24 g scale). The rhodium complex shows the following spectroscopic properties: ^{1}H NMR (400 MHz, CDCl$_3$): δ 5.73 (m, 4H), 4.15 (m, 2H), 2.04 (m, 1H), 1.93 (m, 1H), 1.83 (m, 2H), 1.54 (m, 2H), 1.39 [d, 6H, X-part of an AA′X$_3$X′$_3$ spin system (A = [31]P, X = [1]H, ^2J(P,H) = 8.3 Hz], 1.10 [d, 18H, X-part of an AA′X$_9$X′$_9$ spin system, ^{3}J(P,H) = 14.5 Hz]; ^{13}C NMR (75 MHz, CDCl$_3$, X-parts of an ABMX spin system (A, B = [31]P, M = [103]Rh, X = [13]C): δ 89.5 {J(Rh,C) = 6.7 Hz, [J(P$_A$,C) + J(P$_B$,C)] = 9.2 Hz}, 85.0 {J(Rh,C) = 6.2 Hz, [J(P$_A$,C) + J(P$_B$,C)] = 8.7 Hz}, 72.3 {J(Rh,C) = 3.9 Hz, [J(P$_A$,C + J(P$_B$,C)] = 5.7 Hz}, 56.7 {J(Rh,C) = 1.8 Hz, [J(P$_A$,C) + J(P$_B$,C)] = 3.4 Hz}, 32.3 [J(Rh,C) = 1.6 Hz, J(P$_A$,P$_B$) = 21.4 Hz, J(P$_A$,C) = 25.7 Hz, J(P$_B$,C) = 0.8 Hz], 26.4 [J(P$_A$,C) + J(P$_B$,C)] = 4.2 Hz, 21.5 [J(Rh,C) = 2.8 Hz, J(P$_A$,P$_B$) = 21.4 Hz, J(P$_A$,C) = 27.8 Hz, J(P$_B$,C) = 10.9 Hz], 6.0 [J(Rh,C) = 1.3 Hz, J(P$_A$,P$_B$) = 21.5 Hz, J(P$_A$,C) = 20.8 Hz, J(P$_B$,C) = -0.6 Hz]; ^{11}B NMR (128 MHz, CDCl$_3$): δ 0.0; ^{31}P NMR (121 MHz, CDCl$_3$): δ 62.0 [d, J(Rh,P) = 152 Hz]. The structure was determined by X-ray crystallographic analysis.[2]

17.   The rhodium complex is not readily oxidized on contact with air at room temperature, but it gradually decomposes on prolonged exposure to air. Therefore, storage under argon in a freezer is recommended. The checkers, however, found the complex to be unstable when kept in CD$_3$OD solution.

Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

In contrast to optically active diphosphine ligands bearing a chiral-backbone, C_2-symmetric, P-stereogenic diphosphine ligands, such as (*S,S*)-1,2-bis(alkylmethyl- phosphino)ethane (also known as (*S,S*)-BisP*),[2] have been used only recently as ligands in enantioselective reactions. BisP* was found to be an excellent ligand for enantioselective hydrogenations of olefins or ketones. Its synthesis consists of only three steps starting from *tert*-butyldichlorophosphine. The asymmetric P-center is formed during the

deprotonation step using *sec*-BuLi in the presence of (–)-sparteine.[3] Given the fact that the copper-promoted oxidative coupling[4] of the generated anion proceeds through a radical intermediate, the reaction leading to the (*S,S*) or (*R,R*)-isomers has almost the same rate as that leading to the *meso* compound.[5] Thus, (*S,S*)-BisP*–borane (>99% ee) is contaminated by a small amount of (*R,S*)-BisP*–borane which can be removed by recrystallization.

The (*R,R*)-enantionmer ((*R,R*)-t-Bu-BisP*)) may also be prepared via one of three protocols that we have developed.[6] The recommended method[6c] is reported in the scheme below:

(R,R)-t-Bu-BisP*-borane
98% ee (99% ee after recrystallization)
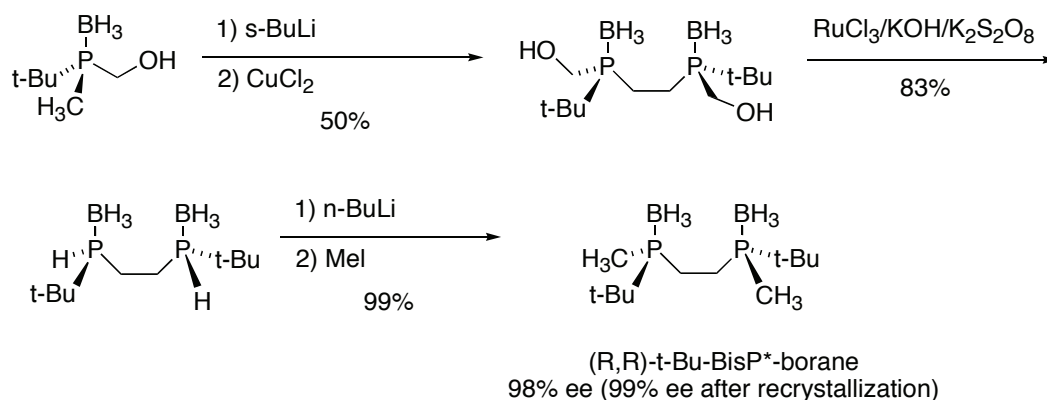
It should be noted that tricoordinate phosphorus compounds in low oxidation states are usually air-sensitive, making their handling and storage difficult. Moreover, chiral phosphines bearing stereogenic phosphorus atoms are prone to racemization especially at higher temperatures[7] and therefore require additional stabilization. Unlike diaryl- and triarylphosphines, however, optically active trialkylphosphines hardly racemize even at elevated temperatures.[8] Temporary protection of the phosphine with BH_3 usually prevents all problems of this kind.[9] The phosphine–borane adducts are air-stable compounds which can be conveniently isolated, purified and stored. Owing to their remarkable inertness and resistance to a wide range of reactions conditions phosphine-borane complexes have emerged as indispensable intermediates for the preparation of P-stereogenic compounds.[10] Cleavage of the P–B bond releases the chiral phosphines with retention of configuration.[5] Complexation with a transition-metal prevents ready oxidation of the ligand.

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5. Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244.
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7. (a) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375; (b) Valentine, D., Jr. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds; Academic Press, Orlando, 1984; Vol. 4; Chapter 3.
8. Baechler, R. D.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 3090.
9. (a) Ohff, M.; Holz, J.; Quirmbach, M.; Börner, A. *Synthesis* **1998**, 1391; (b) Carboni, B.; Monnier, L. *Tetrahedron* **1999**, *55*, 1197.
10. Imamoto, T. *Pure Appl. Chem.* **1993**, *65*, 655.

Appendix
Chemical Abstracts Nomenclature

tert-Butyldichlorophosphine: Phosphonous dichloride, (1,1-dimethylethyl)-; (25979-07-1)

Methylmagnesium bromide: Magnesium, bromomethyl-; (75-16-1)

Borane-tetrahydrofuran: Boron, trihydro(tetrahydrofuran)-, (14044-65-6)

(*tert*-Butyldimethylphosphine)trihydroboron: Boron, [(1,1-dimethylethyl)dimethyl-phosphine]-trihydro-; (203000-43-5)

sec-Butyllithium: Lithium, (1-methylpropyl)-; (598-30-1)

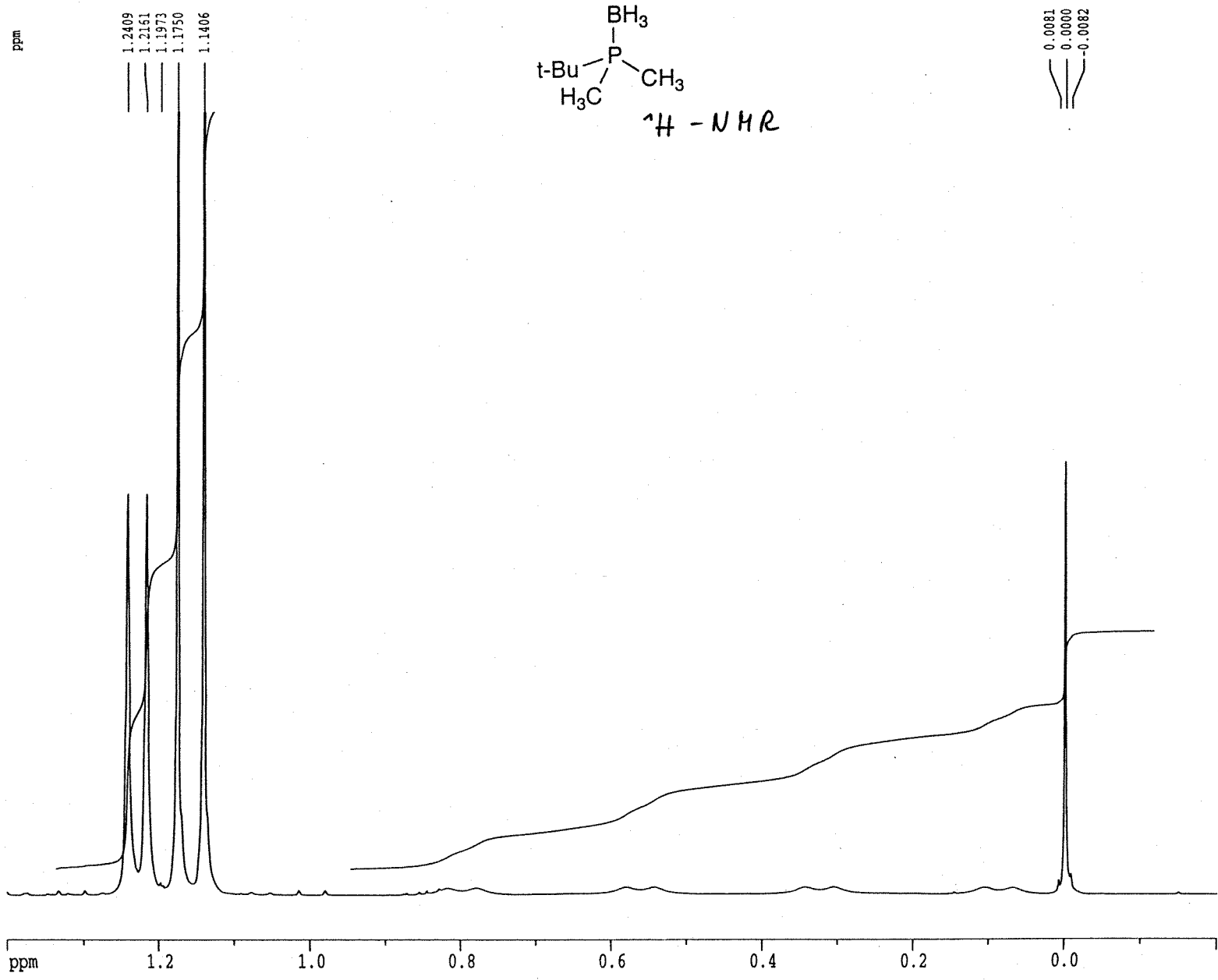Copper (II) chloride: Copper chloride; (7447-39-4)

(-)-Sparteine: 7,14-Methano-2H,6H-dipyrido[1,2-a:1',2'-e][1,5]diazocine, dodecahydro-, (7S,7aR,14S,14aS)-; (90-39-1)
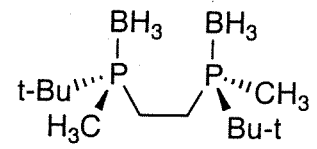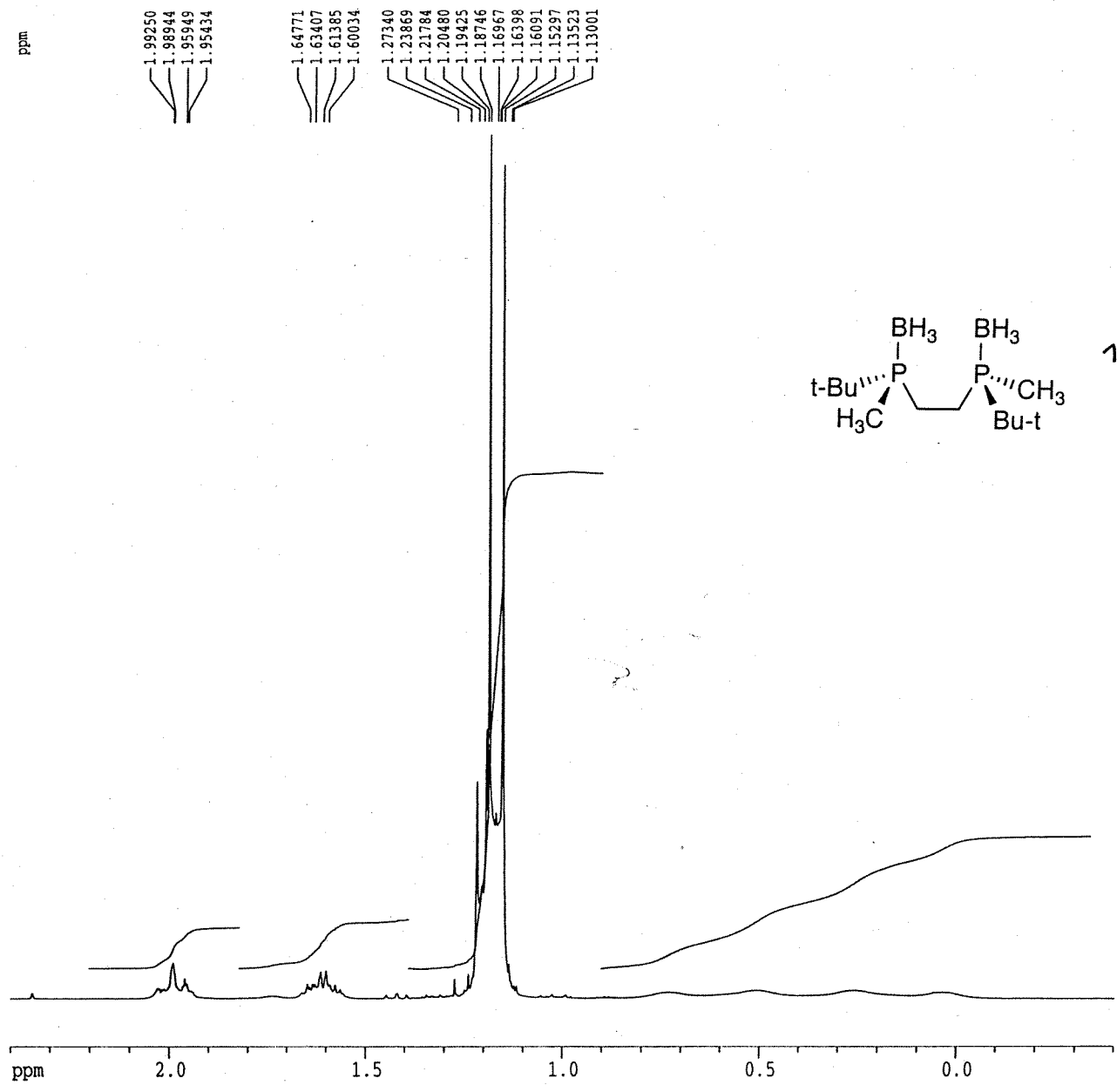
Trifluoromethylsulfonic acid: Methanesulfonic acid, trifluoro-; (1493-13-6)

Potassium hydroxide; (1310-58-3)

(Norbornadiene)rhodium chloride dimer; Rhodium, bis[(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene]di-η-chlorodi-; (12257-42-0)

Rhodium(1+), [(2,3,5,6-η)-bicyclo[2.2.1]hepta-2,5-diene]bis(methyldi-phenylphosphine)-, tetrafluoroborate(1-); (34664-31-8)

ppm

1.2409
1.2161
1.1973
1.1750
1.1406

0.0081
0.0000
-0.0082

BH₃
|
t-Bu—P—CH₃
|
H₃C

¹H – NMR

| ppm | 1.2 | 1.0 | 0.8 | 0.6 | 0.4 | 0.2 | 0.0 |

ppm

1.99250
1.98944
1.95949
1.95434

1.64771
1.63407
1.61385
1.60034

1.27340
1.23869
1.21784
1.20480
1.19425
1.18746
1.16967
1.16398
1.16091
1.15297
1.13523
1.13001

BH₃   BH₃

t-Bu\\\\P   P\\\\\CH₃
      H₃C   Bu-t

¹H - NMR

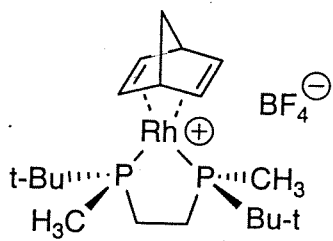ppm   2.0   1.5   1.0   0.5   0.0

Hz
1723.92
1722.88
1721.10
1719.17
1717.92
1716.76
1714.65
1712.65

1446.69

1247.42
1246.11
1244.50
1242.89
1241.53
1239.83

991.93
990.41
988.55

548.13
547.43

467.36
465.92
459.04

419.96
412.52
411.76

339.34
324.75

^{1}H–NMR

BF$_4$ $^{\ominus}$

Rh $\oplus$

t-Bu''''P   P''''CH$_3$

H$_3$C   Bu-t

ppm   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0