Organic Syntheses

Preparation of 2-(2-(Dicyclohexylphosphino)phenyl)-1-methyl-1*H*-indole (CM-phos)

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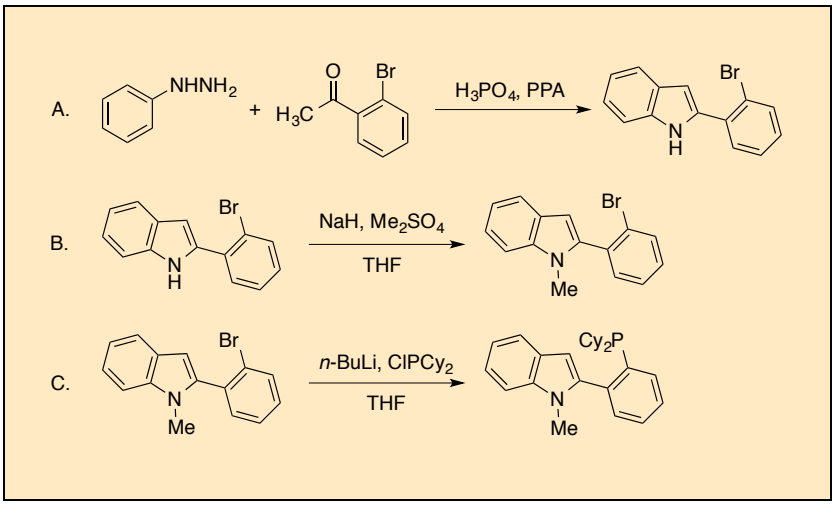

Procedure

A. *2-(2-Bromophenyl)-1H-indole.* An oven-dried 100-mL single-necked round-bottomed flask equipped with a Teflon-coated magnetic stir bar (oval, 25 mm × 15 mm) is charged with 2-bromoacetophenone (2.7 mL, 4.0 g, 20 mmol) (Note 1) and phenylhydrazine (2.4 mL, 2.6 g, 24 mmol) (Note 2) *via* syringe, and stirring is started. Phosphoric acid (10.0 mL) (Note 3) is added slowly over 1 min, and the mixture is stirred for 50 min (Note 4).

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Polyphosphoric acid (56.7 g, Note 5) is added to the reaction mixture slowly over 30 min with continuous stirring (Note 6). The reaction flask is equipped with a Dimroth condenser, and is placed in a pre-heated oil bath (85 ºC). The bath temperature is raised to 120 °C within 1 h under air atmosphere (Note 7). The resulting mixture is stirred at 120 °C for an additional 2 h, and then carefully poured into ice water (90 g ice, 20 mL water) in a 300 mL beaker (Note 8) with stirring by means of a glass rod (Note 9). The remaining crude product in the reaction flask is rinsed with water (3 × 10 mL) (Note 10) and dichloromethane (3 × 10 mL). All rinses are transferred to the beaker. The resulting mixture is stirred by means of a glass rod for 30 min (Note 11), and then poured into 500-mL separatory funnel. The beaker is rinsed with dichloromethane (3 × 10 mL), water (3 × 10 mL), and again dichloromethane (100 mL). All rinses are transferred to the separatory funnel. The funnel is shaken, and the organic layer is separated. The aqueous layer is further extracted with dichloromethane (3 × 100 mL). The combined organic extracts are concentrated by rotary evaporation (37 °C, 52 mmHg). The resulting dark-brown residues are purified by column chromatography (4.5-cm diameter × 16-cm packed height) with 81 g of silica gel (Note 12) in 10% ethyl acetate–hexane (1:9 ethyl acetate:hexane). At this point, 1400 mL is collected with elution of 10% ethyl acetate–hexane (1:9 ethyl acetate:hexane). The eluent containing the product is concentrated by rotary evaporation (37 °C, 20 mmHg) to afford an orange-yellow oil and dried at 7 mmHg for 1 h. This oil is cooled in an ice-water bath, and hexane (20 mL) is added with stirring by means of a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm) for 1 h to afford an off-white powder. The resulting powder is collected by suction filtration on a funnel, washed with ice-cold hexane (3 × 5 mL), dried for 5 h at 0.2 mmHg to provide the crude material as a pale yellow powder (3.5–3.7 g, 64–68%) (Note 13).

The crude powder (3.6 g) is suspended in hexane (20 mL) and vigorously stirred for 1 h with a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm). The resulting white powder is collected by suction filtration on a funnel, washed with ice-cold hexane (3 × 5 mL), and dried for 7 h at 0.2 mmHg to provide 2-(2-bromophenyl)-1*H*-indole (2.3 g, 42%) (Note 14).

B. *2-(2-Bromophenyl)-1-methyl-1H-indole.* An oven-dried 100-mL three-necked round-bottomed flask is equipped with a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm), is charged with sodium hydride (63 % dispersion in mineral oil) (0.46 g of the sodium hydride in oil,

12 mmol) (Note 15). The necks are fitted with a glass stopper, a rubber septum and a nitrogen stopcock inlet. The flask is evacuated and backfilled with nitrogen three times. Sodium hydride is washed free of mineral oil by stirring with distilled hexane (10 mL), and the supernatant liquid is decanted. This operation is repeated for three times. The remaining solvent is removed by placing the flask under vacuum (0.2 mmHg) for 15 min, after which the flask is filled with nitrogen. The glass stopper is removed and 100-mL pressure-equalizing dropping funnel attached (Figure 1). The flask is evacuated and backfilled with nitrogen three times. Anhydrous tetrahydrofuran (5 mL) (Note 16) is added to the reaction flask *via* syringe to form a suspension of sodium hydride, and stirring is started. The suspension is cooled to 0 °C in an ice-water bath.

Figure 1. Apparatus Assembly for Step B

A separate oven-dried 100 mL, two-necked, round-bottomed flask is equipped with a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm) and charged with 2-(2-bromophenyl)-1*H*-indole (2.7 g, 10 mmol). The necks are fitted with a rubber septum and a nitrogen stopcock inlet. The

flask is evacuated and backfilled with nitrogen three times. Anhydrous tetrahydrofuran (20 mL) (Note 16) is added *via* syringe, and stirring is started, to form a solution of 2-(2-bromophenyl)-1*H*-indole. The solution of 2-(2-bromophenyl)-1*H*-indole is transferred to the dropping funnel *via* cannula and additional anhydrous tetrahydrofuran (5 mL) (Note 16) is added to the two-necked flask to rinse all the 2-(2-bromophenyl)-1*H*-indole solution to the dropping funnel. The solution of 2-(2-bromophenyl)-1*H*-indole is added dropwise *via* the dropping funnel to the reaction mixture over 5 min and additional anhydrous tetrahydrofuran (5 mL) (Note 16) is added to the dropping funnel to rinse all the 2-(2-bromophenyl)-1*H*-indole solution to the reaction mixture. Upon completion of the addition, the reaction mixture is allowed to warm to room temperature and stirred for 30 min. Dimethyl sulfate (0.99 mL, 10.3 mmol) (Note 17) is added *via* syringe to the reaction mixture. The mixture is stirred overnight at room temperature, at which time TLC analysis indicates the reaction has been completed (Notes 18 and 19). After adding methanol (5 mL) to quench the excess sodium hydride, the reaction mixture is concentrated by rotary evaporation (36 °C, 20 mmHg) to afford a brown oil. This oil is diluted with ethyl acetate (20 mL), and then transferred to a 300-mL separatory funnel. The reaction flask is rinsed with ethyl acetate (2 × 20 mL), deionized water (2 × 20 mL), and again ethyl acetate (20 mL). All rinses are transferred to the separatory funnel. The funnel is shaken, and the layers are separated. The aqueous phase is separated out and the organic phase is washed with water (2 × 20 mL) and brine (20 mL). The organic extract is concentrated by rotary evaporation (36 °C, 20 mmHg) to afford a brown oil. The oil is purified by column chromatography (3.5-cm diameter × 15-cm packed height) on 50 g of silica gel (Note 12) in 5% ethyl acetate-hexane (1:19 ethyl acetate:hexane). The oil is loaded as a solution in ethyl acetate (2 × 1 mL). At this point, 250 mL of fraction is collected with elution of 5% ethyl acetate-hexane (1:19 ethyl acetate:hexane). The eluent containing the product is concentrated by rotary evaporation (36 °C, 20 mmHg) and dried at 0.2 mmHg for 4 h to afford yellow oil (2.8–2.9 g). The oil contains a small amount of ethyl acetate, which cannot be removed under vacuum (Note 20). The material can be used for the next step after co-evaporation with toluene, as described in Step C.

Alternatively, crystallization of the oil is facilitated by the following process that involves treatment in ethanol. The yellow oil is transferred to a 100 mL, single-necked, round-bottomed flask equipped with a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm). Ethanol (10 mL) is

added to the flask, and stirring is initiated. The mixture is refluxed until a homogenous solution results. The solution is allowed to cool to room temperature, and stirred to afford a white powder (Note 21). The mixture is cooled to 0 °C in an ice-water bath, and stirring is maintained for 10 min. The precipitate is collected by suction filtration on a Büchner funnel, washed with ice-cold ethanol (3 × 5 mL), and dried for 3 h at 0.2 mmHg (Note 22) to provide 2-(2-bromophenyl)-1-methyl-1*H*-indole (2.7 g, 96%) (Note 23) as a white powder.

C. *2-(2-(Dicyclohexylphosphino)phenyl)-1-methyl-1H-indole (*CM-phos*)*. An oven-dried 100-mL three-necked round-bottomed flask is charged with 2-(2-bromophenyl)-1-methyl-1*H*-indole (2.3 g, 8.0 mmol) in the form of the oily material described in Step B. The necks are fitted with two glass stoppers. Anhydrous toluene (2 mL) (Note 24) is added to the flask. The solution is concentrated by rotary evaporation (50 °C, 20 mmHg). This operation is repeated two additional times (Note 25). The flask is equipped with a Teflon-coated magnetic stir bar (cylindrical, 25 mm × 8 mm), glass stoppers are changed to 50-mL pressure-equalizing dropping funnel, rubber septum, and nitrogen stopcock inlet. The flask is evacuated and backfilled with nitrogen three times. Anhydrous tetrahydrofuran (40 mL) (Note 16) is added to the reaction flask *via* syringe to form a solution of 2-(2-bromophenyl)-1-methyl-1*H*-indole and stirring is started. The solution is cooled to –78 °C in a dry ice-acetone bath. *n*-Butyllithium (5.4 mL, 1.63 M in hexane, 8.8 mmol) (Note 26) is added dropwise *via* dropping funnel over 3 min and additional anhydrous tetrahydrofuran (2 mL) (Note 16) is added to the dropping funnel to rinse all the *n*-butyllithium solution into the reaction mixture. The resulting mixture is stirred for an additional 30 min at –78 °C. Chlorodicyclohexylphosphine (2.2 mL, 9.6 mmol) (Note 27) and anhydrous tetrahydrofuran (5 mL) (Note 16) are added to the dropping funnel to form a solution of chlorodicyclohexylphosphine. The solution is added dropwise *via* dropping funnel at –78 °C over 3 min, and additional anhydrous tetrahydrofuran (2 mL) (Note 16) is added to the dropping funnel to rinse all phosphine solution to the reaction mixture. The resulting mixture is allowed to warm to room temperature within 2 h and stirred for overnight at 22 °C, at which time TLC analysis indicates completion of the reaction (Notes 18 and 28). After adding methanol (5 mL) to quench the excess *n*-butyllithium, the reaction mixture is concentrated by rotary evaporation (36 °C, 20 mmHg) and dried at 0.2 mmHg for 15 min to afford an off-white solid. This solid is cooled in an ice-water bath, and methanol (20 mL) is added with stirring for 30 min to afford an off-white powder.

The resulting powder is collected by suction filtration on a Büchner funnel, washed with ice-cold methanol (2 × 5 mL) and ice-cold hexane (5 mL), and dried for 3 h at 0.2 mmHg to give 2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-1*H*-indole (CM-phos) (2.2–2.4 g, 69–75%) (Notes 29 and 30) as a white powder.

Notes

1. 2-Bromoacetophenone (>98%) was obtained from Tokyo Chemical Industry Co., Ltd. (TCI) (checkers). 2-Bromoacetophenone (99%) was obtained from Aldrich Co., Inc. and used as received (submitters).
2. Phenylhydrazine (>98%) was obtained from Tokyo Chemical Industry Co., Ltd. (TCI) (checkers). Phenylhydrazine (97%) was obtained from Acros Organics and used as received (submitters).
3. Phosphoric acid (ACS reagent, ≥85% H_3PO_4) was obtained from Aldrich Co., Inc. and used as received.
4. Upon addition of phosphoric acid, the reaction mixture solidified, and the color changed from clear pale-yellow to turbid yellow. After heat was released, the solid started to disappear and the reaction mixture was allowed to stir for 30 min until the reaction mixture reached room temperature.
5. Polyphosphoric acid (reagent grade, 115% H_3PO_4 basis) was obtained from Aldrich Co., Inc. and used as received.
6. Since polyphosphoric acid is a viscous liquid, it was first weighed in a beaker, and then transferred to the reaction flask slowly over 10 min. Notably, not all polyphosphoric acid in the beaker could be transferred to the reaction flask, the amount of polyphosphoric acid could be determined by weight difference of the beaker before and after addition. If the polyphosphoric acid is added too quickly, the reaction mixture becomes very viscous and is unable to be stirred with the stir bar. If needed, the mixture can be mixed thoroughly by glass rod or overhead stirring.
7. The color of the reaction mixture was changed from yellow to dark-green to dark-brown. The reaction mixture should be efficiently stirred during heating, otherwise uneven-heating of the reaction mixture will occur, resulting in lower yield.
8. Precaution: Heat insulated gloves should be put on when pouring the hot reaction mixture into ice water.

9. Overhead stirring could also be employed.
10. Grey precipitates were formed when the crude product was added to ice water.
11. To make the mixture less viscous, thorough stirring by a glass rod is necessary, otherwise a huge amount of product will be lost. Overhead stirring could also be employed.
12. Silica gel 60N (Spherical, neutral, 63–210 μm) was obtained from KANTO CHEMICAL Co., Inc. (checkers). Silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM) was obtained from Merck Millipore and used as received (submitter).
13. Checkers noted that the product is contaminated by the remaining starting material (2–8%).
14. Melting point: 76.7–77.3 °C; IR (cm^{-1}) 3382, 3053, 1614, 1559, 1463, 1447, 1435, 1401, 1355, 1301, 1229, 1178, 1115, 1073, 1022, 958, 942, 931, 849, 795, 745, 721, 695, 676, 644, 609; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 6.82 (s, 1H), 7.14 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.22 (dd, 1H, *J* = 8.4, 7.8 Hz), 7.23 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.39 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.43 (d, 1H, *J* = 8.4 Hz), 7.62 (d, 1H, *J* = 7.8 Hz), 7.67 (d, 1H, *J* = 7.8 Hz), 7.69 (d, 1H, *J* = 7.8 Hz), 8.65 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 103.7, 111.0, 120.2, 120.8, 121.3, 122.6, 127.7, 128.2, 129.2, 131.5, 133.5, 134.0, 136.3; HRMS calcd. for $C_{14}H_{10}NBrH^+$: 272.0069, found 272.0065; Anal. calcd. for $C_{14}H_{10}NBr$: C, 61.79; H, 3.70; N, 5.15. found: C, 62.01; H, 3.56; N, 5.17; R_f = 0.23 in 10% ethyl acetate–hexane (1:9 ethyl acetate:hexane) solvent system.
15. Sodium hydride (63 % dispersion in mineral oil) was obtained from Yoneyama Yakuhin Kogyo. Co., Ltd., (checkers). Sodium hydride (60 % dispersion in mineral oil) was obtained from Aldrich Co., Inc. (submitters).
16. Tetrahydrofuran (anhydrous) was obtained from KANTO CHEMICAL Co., Inc. (checkers). Tetrahydrofuran (ACS grade) was obtained from Tedia and distilled from sodium benzophenone ketyl under nitrogen (submitters).
17. Dimethyl sulfate (>98%) was obtained from Tokyo Chemical Industry Co., Ltd. (TCI) (checkers) and Aldrich Co., Inc. (submitters), and used as received.
18. Thin layer chromatography was performed on pre-coated TLC-plates (Merck Co., Inc. TLC silica gel 60 F_{254}, Art 5715, 0.25 mm) (checkers). Thin layer chromatography was performed on pre-coated TLC-sheets ALUGRAM® SIL G/UV254 and obtained from MACHEREY-NAGEL GmbH & Co. KG (submitters).

19. The R_f value of 2-(2-bromophenyl)-1-methyl-1*H*-indole: 0.56 (1:9 ethyl acetate:hexane).
20. Checkers noted that the oil contained ethyl acetate (4–6%), which cannot be removed even after prolonged standing under vacuum (0.2 mmHg, 4 h).
21. Crystallization of the oil is facilitated in ethanol. Ethanol (99.5 %) was obtained from Nacalai Tesque Co. (checkers) and VWR (submitters), and used as received. The time required for the precipitation varies from 10 min (submitters) to 2–3 days (checkers).
22. In preparation for use in the next step, the precipitate should be well dried (0.2 mmHg, 3 h). By this protocol, ethanol was no longer detected by ^{1}H NMR.
23. Melting point: 92.2-92.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.57 (s, 3H), 6.51 (s, 1H), 7.15 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.27 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.29–7.33 (m, 1H), 7.35–7.43 (m, 3H), 7.66 (d, 1H, *J* = 7.8 Hz), 7.71 (d, 1H, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 30.6, 102.1, 109.5, 119.8, 120.7, 121.8, 125.2, 127.2, 127.6, 130.1, 132.8, 132.9, 134.3, 137.3, 139.7; IR (cm^{-1}) 3053, 2937, 1924, 1560, 1542, 1463, 1431, 1386, 1360, 1339, 1311, 1235, 1204, 1165, 1145, 1130, 1098, 1058, 1024, 1004, 947, 923, 896, 783, 762, 749, 738, 689, 665, 643, 579, 536; HRMS calcd. for $C_{15}H_{12}NBrH^+$: 286.0231, found 286.0221.
24. Toluene was obtained from KANTO CHEMICAL Co., Inc. (checkers).
25. Treatment with toluene and evaporation of the toluene is not necessary if crystalline material is used.
26. *n*-Butyllithium (1.6 M solution in hexane) was obtained from KANTO CHEMICAL Co., Inc. and used as received (checkers). *n*-Butyllithium (1.6 M solution in hexane) was obtained from J&K Chemical Co. and titrated with 1,3-diphenylacetone *p*-tosylhydrazone in anhydrous tetrahydrofuran under nitrogen prior to use, the *n*-butyllithium was titrated[2] to be 1.32 M (submitters).
27. Chlorodicyclohexylphosphine (97%) was obtained from Aldrich Co., Inc. and used as received.
28. The R_f value of CM-phos is 0.59 (ethyl acetate:hexane ,1:9).
29. Melting point: 181.2–182.4 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ: 1.05–1.36 (m, 11H), 1.62–1.85 (m, 11H), 3.50 (s, 3H), 6.39 (s, 1H), 7.14 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.24 (dd, 1H, *J* = 8.4, 7.2 Hz), 7.35–7.42 (m, 2H), 7.47 (dd, 1H, *J* = 7.8, 7.2 Hz), 7.52 (t, 1H, *J* = 7.2 Hz), 7.62 (d, 1H, *J* = 7.8 Hz), 7.70 (brd, 1H, *J* = 5.4 Hz); ^{13}C NMR (150 MHz, CD_2Cl_2) δ: 26.4, 27.2, 30.66, 30.69, 103.0, 103.1, 109.3, 119.3, 120.0, 120.9, 127.7, 128.0, 128.1, 131.6, 131.7,

132.77, 132.80, 136.6, 137.5, 137.6, 140.8, 141.0, 141.5, 141.6 (unresolved complex C-P splittings were observed); ^{31}P NMR (243 MHz, CD_2Cl_2) δ: –9.96; IR (cm^{-1}) 3054, 2923, 2847, 1539, 1467, 1445, 1419, 1385, 1363, 1339, 1310, 1265, 1234, 1199, 1179, 1167, 1145, 1122, 1099, 1000, 920, 886, 849, 778, 768, 745, 731, 670; HRMS calcd. for $C_{27}H_{34}NPH^+$: 404.2501, found 404.2513; Anal. calcd. for $C_{27}H_{34}NP$: C, 80.36; H, 8.49; N, 3.47. found: C, 80.53; H, 8.15; N, 3.47.

30. CM-phos was stored with an argon atmosphere in the cool and dark space.

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Discussion

It is well known that ligand design and synthesis are very important for the metal-catalyzed coupling reactions. After recognizing the preliminary relationship between the ligand structure and the outcome of the coupling reaction, various research groups have designed and synthesized countless supporting ligands for the coupling reactions, such as P*t*-Bu_3,[3] Buchwald ligand kit,[4] and Josiphoskit.[5] Although a variety of ligands have been developed, rapid assembly of structurally diverse ligand systems via simple synthetic methods is still important for the development of versatile catalysts for more widespread applications of coupling reactions.

We have the following strategic considerations for the design of effective ligands for the coupling reactions: (1) the starting materials should be inexpensive and readily available; (2) the ligand synthesis should be simple and straightforward (an elimination of metal/halogen exchange (from ArBr or ArI) would be even more advantageous); (3) the ligand diversity should be easily accessible, and should conveniently provide high level of steric and electronic fine-tunings. Based on these three strategies, indole was selected as template to design and explore a new class of phosphine ligands. There were several reasons for the choice of indole: (1) indole and starting materials to synthesize indole derivatives, such as phenylhydrazine and acetophenone are generally inexpensive; (2) indole and most of its derivatives are readily and commercially available; (3) many synthetic methods of indoles have been reported for over hundreds of years,[6] such as Fischer indole synthesis and metal-catalyzed indole synthesis.

Notably, the chemical properties of indole scaffold can provide potential for diversification of the new ligands. One of the modern concepts for the phosphine ligand design is the rapid assembly of the two major compartments. One compartment is the phosphorus atom that attaches two of the simple equivalent groups that can be an aryl or alkyl group, such as diphenyl or dicyclohexyl group. Another compartment is the ligand template that provides steric and electronic fine-tuning for the phosphine ligand. Herein, CM-phos that derived from indole ligand template was highly tunable in both steric and electronic effects (Figure 2).

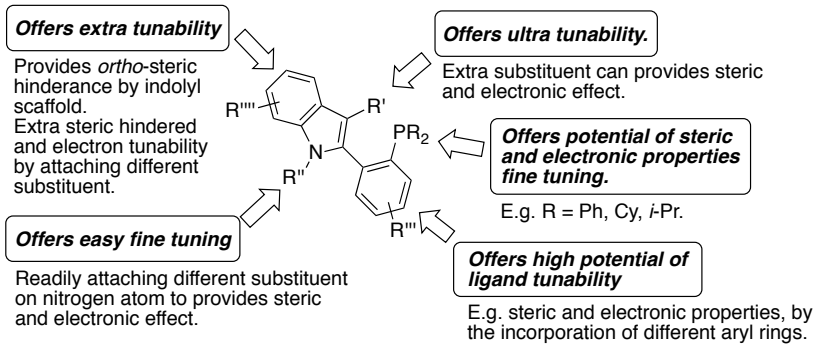

Figure 1. Ligand design and diversity

To sum up, the indole ligand template 1) is inexpensive; 2) can be readily available from commercially accessible starting materials; 3) can be synthesized from well-developed synthesis methods; and 4) has high potential for diversification and easy steric and electronic fine-tuning.

We finally selected the Fischer indole synthesis[6b] as our primary tool to synthesize the indole templates from phenylhydrazine and 2′-bromoacetophenone. With the methylated ligand precursor, CM-phos could be afforded easily by lithiation and subsequently trapping with chlorodicyclohexylphosphine. It should be noted that CM-phos in combination with the precatalyst palladium(II) acetate is highly active and effective in amination and Suzuki cross-coupling reaction of aryl mesylates.[7]

References

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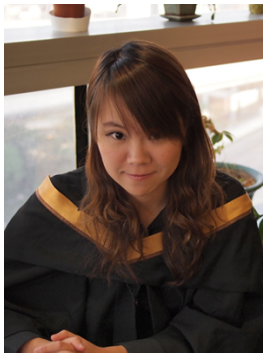
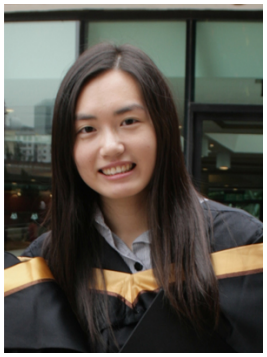
Appendix
Chemical Abstracts Nomenclature (Registry Number)

2′-Bromoacetophenone; (2142-69-0)
Phenylhydrazine; (100-63-0)
Phosphoric acid; (7664-38-2)
Polyphosphoric acid; (8017-16-1)
Sodium hydride; (7646-69-7)
Dimethyl sulfate; (77-78-1)
n-Butyllithium; (109-72-8)
Chlorodicyclohexylphosphine; (16523-54-9)

Shun Man Wong received his B.Sc. in chemical technology from The Hong Kong Polytechnic University in 2010. He pursued his postgraduate study at the same university and obtained his Ph.D. degree in 2014. He is currently a postdoctoral fellow under the supervision of Prof. Fuk Yee Kwong, researching the synthesis of new heterocyclic phosphine ligands and their potential applications.

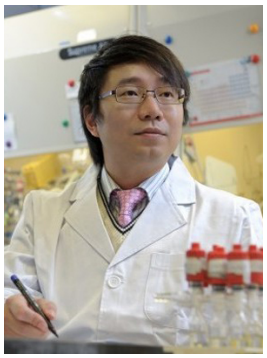


On Ying Yuen received her B.Sc. (1st class honor) in Chemical Technology from the Hong Kong Polytechnic University in 2011. Currently, she is pursuing her Ph.D. under the guidance of Prof. Fuk Yee Kwong. Her main research focuses on palladium-catalyzed direct functionalization of aromatics: process and catalyst design.



Pui Ying Choy received her B.Sc. in Chemical Technology in The Hong Kong Polytechnic University in 2010. She pursued her postgraduate study at the same university and obtained her Ph.D. degree in 2014. She is currently a research associate under the supervision of Prof. Fuk Yee Kwong, researching the synthesis of new heterocyclic phosphine ligands and their potential applications in transition-metal catalysis.

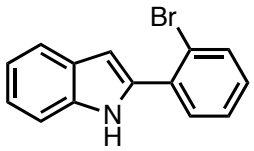
Chau Ming So is currently a Visiting Assistant Professor in the Department of Applied Biology and Chemical Technology of The Hong Kong Polytechnic University. He received his B.Sc. (1st class honor) from PolyU in 2006. He pursued his postgraduate study at the same university and obtained his Ph.D. degree in 2010. He received the Hong Kong Young Scientist Award in the same year. Moreover, he was the winner of Eli Lilly the Best Thesis Award (1st Prize). In 2012-2013, he moved to Institute of Materials Research and Engineering (IMRE) as postdoctoral fellow in Prof. Tamio Hayashi's research group.



Fuk Yee (Michael) Kwong is currently a professor of the Department of Applied Biology and Chemical Technology at The Hong Kong Polytechnic University. He received his B.Sc. in 1996, and completed his Ph.D. at The Chinese University of Hong Kong in 2000 under the supervision of Professor Kin Shing Chan. In 2001–2003, he was at the Massachusetts Institute of Technology (MIT), USA, as a Croucher Foundation postdoctoral fellow. Kwong's research interests are in the areas of new crosscoupling methodologies, carbon–hydrogen bond functionalization, and catalytic enantioselective transformations.

Takumi Fukazawa was born in Chiba, Japan. He received his B. Sc. degree in 2012 at Waseda University under the supervision of Prof. Kuniaki Tatsuta. In the same year, he joined the research group of Prof. Keisuke Suzuki at Tokyo Institute of Technology. In 2014, he received his M. Sc., and currently is pursuing his Ph.D. degree.

2-(2-bromophenyl)-1H-indole
1H CDCl3



BRUKER

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FIDRES             0.183399 Hz
AQ                 2.7263477 sec
RG                     31.94
DW                     41.600 use
DE                     10.00 use
TE                     300.0 K
D1                 1.00000000 sec
TD0                        1

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NUC1                       1H
P1                     12.00 use
PLW1           23.00000000 W

F2 - Processing parameters
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GB           0
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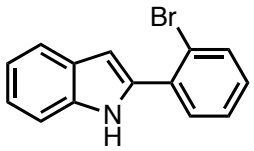
2-(2-bromophenyl)-1H-indole
13C CDCl3



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128.199
127.727
122.623
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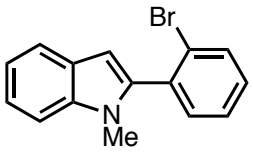
120.825
120.194
111.027
103.648
77.228
77.017
76.805
0.000

BRUKER
No parameters

2-(2-bromophenyl)-1-methyl-1H-indole
1H CDCl3



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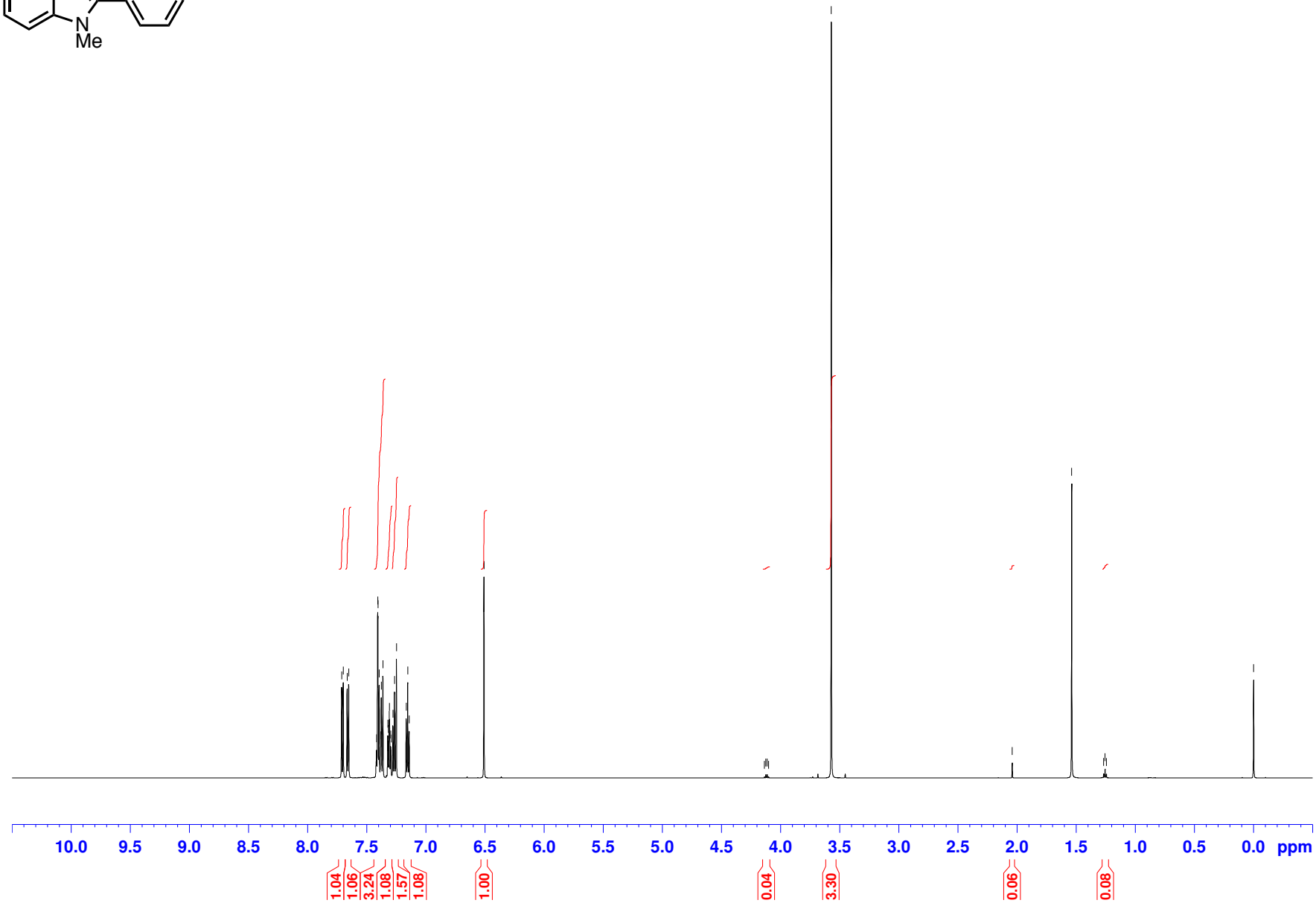

BRUKER

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DS                         2
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FIDRES             0.183399 Hz
AQ                 2.7263477 sec
RG                     31.94
DW                     41.600 use
DE                     10.00 use
TE                     300.0 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 =======
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NUC1                    1H
P1                     12.00 use
PLW1           23.00000000 W

F2 - Processing parameters
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SSB          0
LB                      0.30 Hz
GB           0
PC                      1.00
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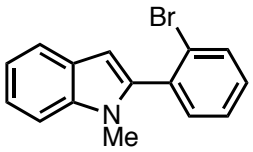
2-(2-bromophenyl)-1-methyl-1H-indole
13C CDCl3



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137.258
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132.860
132.769
130.123
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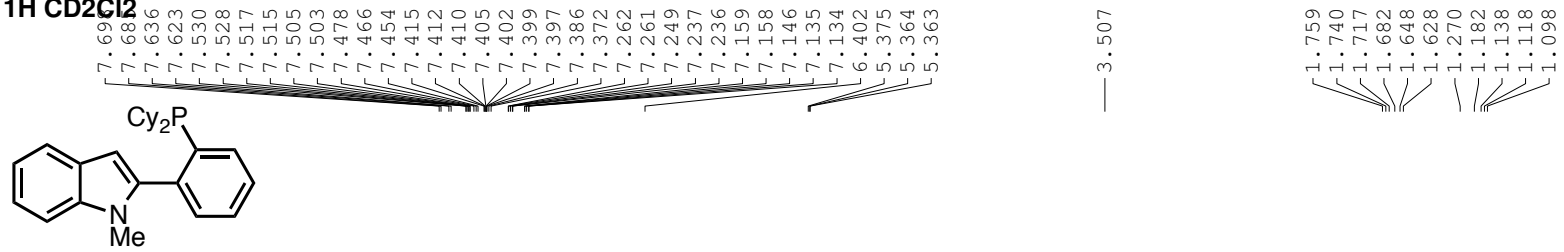
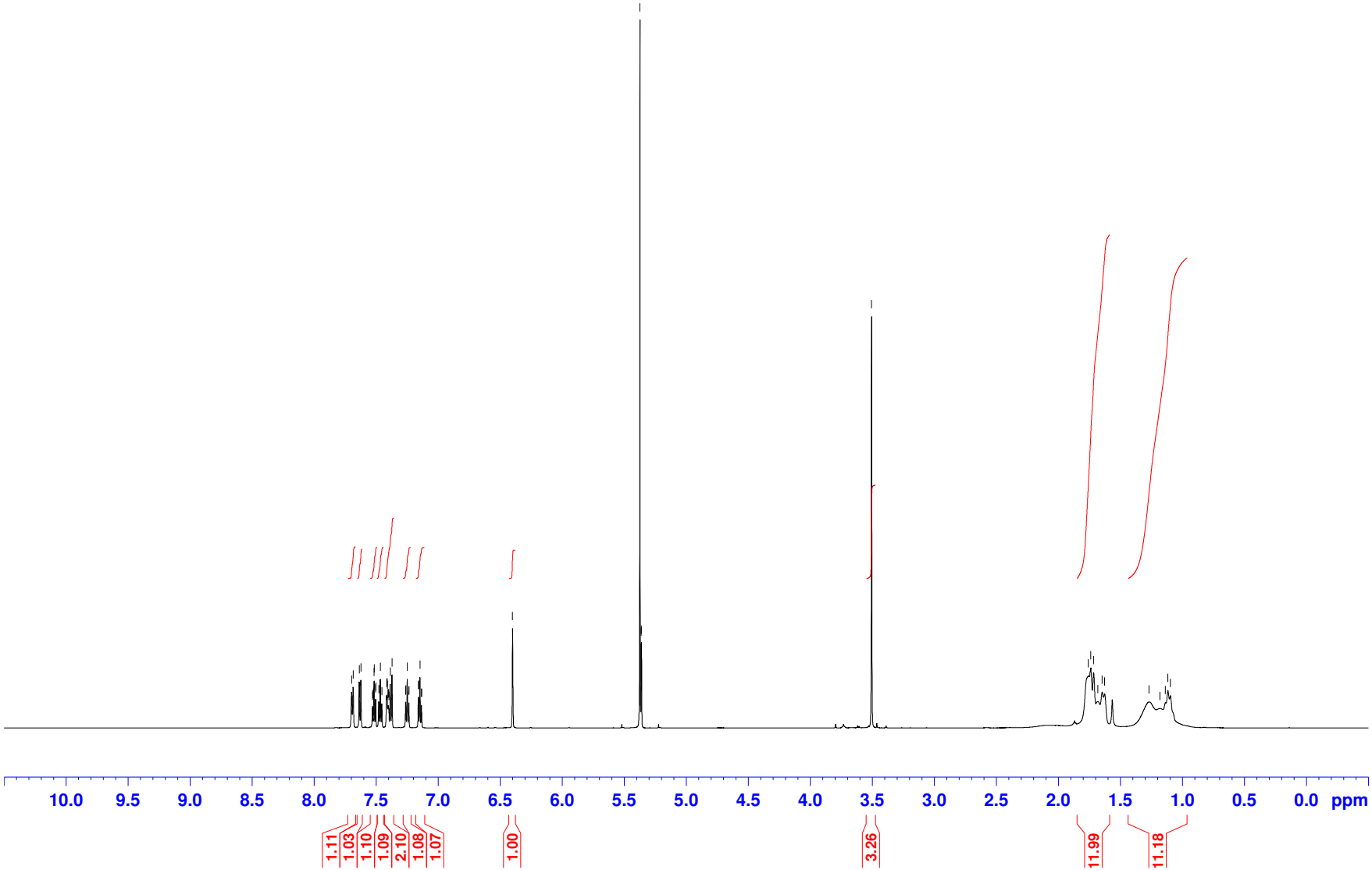
127.177
125.190
121.752
120.723
119.762
109.522
102.113
77.224
77.012
76.801
30.644
0.004

No parameters

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-1H-indole (CM-phos)
1H CD2Cl2



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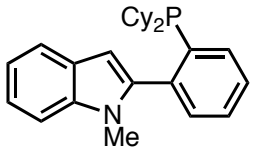
DS                          2
SWH               12019.230 Hz
FIDRES            0.183399 Hz
AQ                2.7262976 sec
RG                      17.5
DW                    41.600 use
DE                    10.00 use
TE                    300.0 K
D1              1.00000000 sec
TD0                         1

======== CHANNEL f1 =======
SFO1           600.1337060 MHz
NUC1                     1H
P1                    12.00 use
PLW1           23.00000000 W

F2 - Processing parameters
SI                     65536
SF             600.1300000 MHz
WDW                       EM
SSB       0
LB                     0.30 Hz
GB        0
PC                     1.00
```

2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-1H-indole (CM-phos)
13C CD2Cl2



BRUKER

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PROCNO                      1

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TD                      65536
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NS                        256
DS                          4
SWH                36057.691 Hz
FIDRES              0.550197 Hz
AQ                  0.9087659 sec
RG                     175.56
DW                     13.867 use
DE                     18.00 use
TE                     300.0 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                         1

======== CHANNEL f1 =======
SFO1             150.9178981 MHz
NUC1                    13C
P1                    10.00 use
PLW1            70.00000000 W

======== CHANNEL f2 =======
SFO2             600.1324005 MHz
NUC2                    1H
CPDPRG[2             waltz16
PCPD2                 70.00 use
PLW2            26.00000000 W
PLW12            0.76407999 W
PLW13            0.37439999 W

F2 - Processing parameters
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SF               150.9028090 MHz
WDW                        EM
SSB          0
LB                     1.00 Hz
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PC                     1.40
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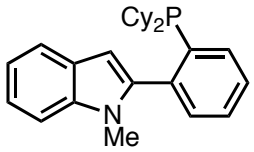
2-(2-(dicyclohexylphosphino)phenyl)-1-methyl-1H-indole (CM-phos)
31P CD2Cl2

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PROCNO                     1

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Time                   21.48
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PULPROG                zgpg30
TD                      65536
SOLVENT                CD2Cl2
NS                        256
DS                          4
SWH                 96153.844 Hz
FIDRES               1.467191 Hz
AQ                   0.3407872 sec
RG                      175.56
DW                       5.200 use
DE                      18.00 use
TE                      300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                         1

======== CHANNEL f1 =======
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NUC1                      31P
P1                      12.00 use
PLW1              60.00000000 W

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NUC2                      1H
CPDPRG[2              waltz16
PCPD2                   70.00 use
PLW2              26.00000000 W
PLW12              0.76407999 W
PLW13              0.37439999 W

F2 - Processing parameters
SI                        32768
SF                242.9370770 MHz
WDW                        EM
SSB           0
LB                      1.00 Hz
GB            0
PC                      1.40
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