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Asymmetric synthesis of a chiral diarsine ligand via a cycloaddition reaction between 3,4-dimethyl-1-phenylarsole and diphenylvinylarsine

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ABSTRACT

The organopalladium complex containing *ortho*-metallated (*S*)-[1-(dimethylamino)ethyl]naphthalene as a chiral auxiliary has been successfully employed to promote the asymmetric cycloaddition reaction between 3,4-dimethyl-1-phenylarsole and diphenylvinylarsine. In the intramolecular cycloaddition reaction, a pair of separable diastereomeric palladium complexes was obtained in the ratio of 6:1. The chiral naphthylamine auxiliary could be removed chemoselectively from the template by treatment with HCl and subsequently NaI to generate the neutral diiodo complex [(As–As)PdI_2]. Treatment of the diiodo complex with KCN gave the enantiomerically pure As–As bidentate ligand in quantitative yield. In contrast to the reported similar P–P and As–P analogues, both arsenic donors in the diiodo complex could be readily eliminated to produce a structurally novel dimetallic complex.

1. Introduction

Since the organoarsenic compound 'Salvarsan'[1–3] was used as a modern chemotherapeutic agent at the beginning of the 1910s, which led to the rapid expansion of arsenic chemistry, arsine ligands have been found to be more active and selective than the corresponding phosphines in many transition-metal-catalysed organic reactions, due to their poorer σ-donor ability.[4–9] Subsequently much attention has been devoted to the study of the enantiomerically pure arsine compounds, for example the chiral *R*-ethylmethylpropylarsine can be obtained with 60% enantiomeric purity by reductive methylation of ethylpropylarsinic acid and trapping by a palladium complex.[10] The phosphine ligand (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) (BINAP) is widely used in asymmetric synthesis. The chiral arsine analogue of BINAP, 2,2′-bis(diphenylarsino)-1,1′-binaphthyl (BINAs) was found to be an effective ligand for an alkenyl iodide-using an intramolecular asymmetric Heck reaction.[11]

In contrast to the many chiral phosphine-based ligands that have been synthesized, relatively few arsine ligands have been prepared and applied in organic reactions or medicine etc, particularly chiral diarsine ligands.[12–16] In studies concerning the preparation and stereochemistry of chiral arsine ligands, several types of As–N, As–S, As–P and As–As bidentate ligands have been resolved via metal complexation techniques,[17,18] although the resolution process has the limitation of a 50% yield for the separation of one enantiomer and could become relatively inefficient when the target ligand has more than one stereogenic centre. In view of our interest in the synthesis and resolution of chiral arsines, we have recently reported on the asymmetric synthesis of a series of As–P bidentate ligands using the well-known Diels–Alder reaction which could be used to produce five stereogenic centres in one step.[19–25] We wondered if the above synthetic method could be extended to the preparation of chiral As–As bidentate ligands. Herein we report on the asymmetric synthesis of a chiral diarsine ligand via the cycloaddition reaction between 3,4-dimethyl-1-phenylarsole and diphenylvinylarsine using the organopalladium complex as a chiral promoter.

2. Results and discussion

2.1. Synthesis of a chiral diarsine ligand

Since the Pd–Cl bond in (+)-**1** is thermodynamically stable and kinetically inert, the chloro ligand in (+)-**1** was replaced with

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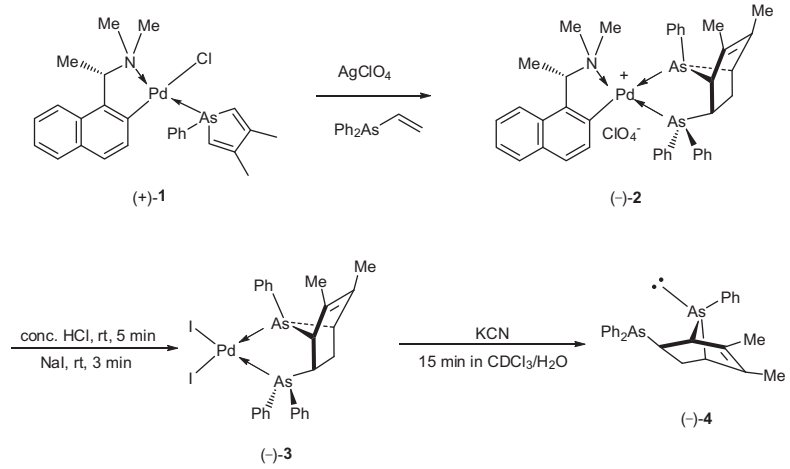


Scheme 1.

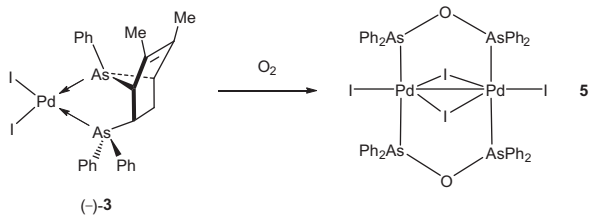
perchlorate by using $AgClO_4$ in dichloromethane in quantitative yield.[27] The asymmetric cycloaddition reaction between the resulting intermediate perchlorate complex and diphenylvinylarsine was completed in 24 h at 40 °C and resulted in the formation of two diastereomers in a ratio of 6:1 (Scheme 1). The major isomer (−)-**2** was isolated by column chromatography in 75% yield, $[\alpha]_D = -91.8$ (*c* 0.49, CH_2Cl_2), and was then recrystallized from chloroform–diethyl ether in the form of pale yellow needles. The Diels–Alder reaction was further proven by ^1H NMR spectrum in which the chemical shift of the proton of the double bond in DMPA of (+)-**1** was changed from 6.69 and 6.97 ppm[20] to 2.95 and 3.80 ppm.

The chiral amine auxiliary on complex (−)-**2** can be removed from the template complex chemoselectively using concentrated HCl for 5 min at room temperature. The resultant dichloro complex is very unstable in solution and therefore it is very difficult to purify by column chromatography or fractional crystallization. Hence it was further converted into the corresponding diiodo complex (−)-**3** by treatment with NaI for 3 min at room temperature. The diiodo complex (−)-**3** was readily isolated by column chromatography in 70% yield, $[\alpha]_D = -78.6$ (*c* 0.14, CH_2Cl_2).

Due to the configurational instability of the uncoordinated As–As bidentate ligand, the liberation process must be carried out under strictly inert atmospheric conditions. A mixture of (−)-**3** and excess KCN in $CDCl_3$ and H_2O was shaken vigorously for 15 min at room temperature to liberate the optically active bidentate ligand (−)-**4** as an air-sensitive solid in quantitative yield, $[\alpha]_D = -81.7°$ (*c* 6.16, $CDCl_3$).

2.2. Arsenic elimination reaction

During the recrystallization of diiodo complex (−)-**3**, deep red crystals were obtained (Scheme 2). From the X-ray structural analysis of this complex, however, it was evident that this was not the original diiodo complex (−)-**3**; on the contrary an unexpected complex **5** was obtained (Fig. 1). Selected bond lengths and angles are listed in Table 2.



Scheme 2.

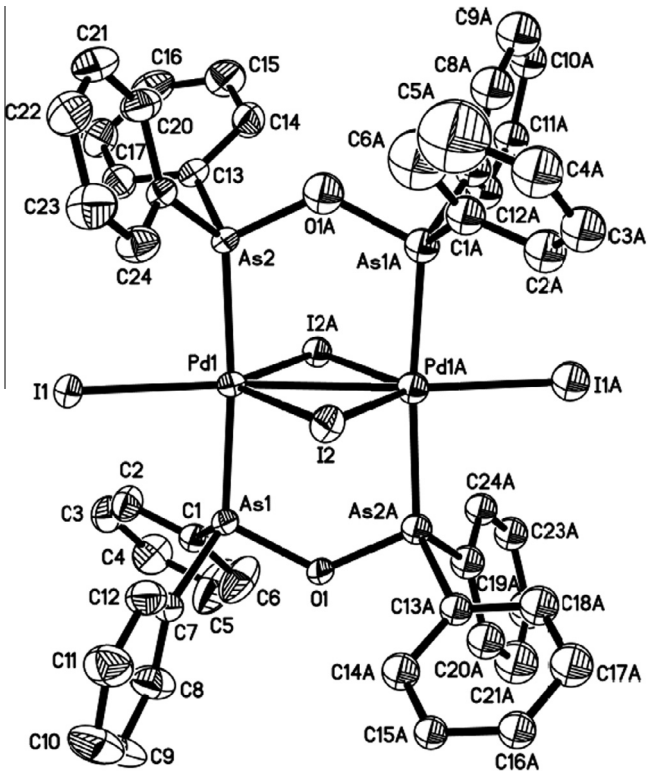


Figure 1. Molecular structure of complex **5**.

All three As–C bonds in the As–As bidentate arsanorbornene skeleton undergone cleavage. This is in contrast to the analogous As–P dichloro and dibromo complexes in which case only the bridged head arsenic atom collapsed, while the P was still retained.[19–21] The coordination about each Pd atom is a distorted octahedron. Analysis of the X-ray data showed that the two diphenylarsine ligands occupy the axial positions, whereas the terminal iodo ligand, the two bridging iodo ligands and another palladium metal can be considered to occupy the equatorial positions. The two neighbouring side by side diphenylarsine groups were linked via an oxygen bridge. This further proves that As—C bonds are

generally much weaker than their P–C counterparts. The Pd—As bond length [2.379(1) Å] in **5** is in the range of those bond distances observed in similar complexes.[19–25] The As–O bond [1.785(2) Å] is nearly identical to a reported corresponding bond [1.786(4) Å].[21] The lengths of three Pd—I bonds [2.665(1), 2.743(1) and 2.954(1) Å] in **5** are longer than the reported Pd–I bonds of the similar diiodide palladium complexes [2.620(1)–2.660(1) Å] [19,21]. The As—Pd—As bond angle [173.8(1)°] is almost linear.

3. Conclusion

In conclusion, we have successfully synthesized a new enantiomerically pure As–As bidentate compound in moderate selectivity via the asymmetric cycloaddition reaction between 3,4-dimethyl-1-phenylarsole and diphenylvinylarsine. It was found that the arsenic elimination reaction was observed in the resultant diiodo complex [(As–As)PdI_2] in which three As—C bonds collapsed to produce a new dimetal complex.

4. Experimental

4.1. General

Reactions involving air-sensitive compounds were performed under an inert atmosphere of argon using standard Schlenk techniques. Solvents were dried and freshly distilled according to standard procedures and degassed prior to use when necessary. NMR spectra were recorded at 25 °C on Bruker Avance 400 and 500 spectrometers. Optical rotations were measured on the specified solution in a 0.1 dm cell at 20 °C with a Perkin–Elmer 341 polarimeter and the units are deg cm^2 g^{-1}. Elemental analysis was performed by the Elemental Analysis Laboratory of the Division of Chemistry and Biological Chemistry at Nanyang Technological University. Melting points were measured on a Stanford Research Systems OptiMelt MPA 100 instrument and are uncorrected. Diphenylvinylarsine[26] and (+)-**1**[20] were prepared following literature procedures. **Caution!** Perchlorate salts of metal complexes are potentially explosive compounds and should be handled with care.

4.2. Cycloaddition reaction: preparation of complex (−)-2

A solution of (+)-**1** (0.63 g, 1.10 mmol) in dichloromethane (30 mL) was stirred for 2 h in the presence of a solution of silver perchlorate (0.40 g) in water (1 mL). The organic layer, after removal of AgCl, was then washed with water (3 × 50 mL), dried ($MgSO_4$) and subsequently treated with diphenylvinylarsine (0.28 g, 1.10 mmol) at 40 °C for 24 h. The solvent was removed from the reaction mixture, and complex (−)-**2** was isolated by column chromatography on a silica column with dichloromethane–diethyl ether to give a pale yellow solid, which was recrystallized from chloroform–diethyl ether in the form of needles (0.74 g, 75%). $[\alpha]_D$ = −91.8 (*c* 0.49, CH_2Cl_2). Mp: 152–153 °C. Anal. Calcd for $C_{40}H_{42}As_2ClNO_4Pd$: C, 53.8; H, 4.7; N, 1.6. Found: C, 53.6; H, 4.9; N, 1.6. ^{1}H NMR ($CDCl_3$, δ): 1.41 (s, 3H, =C*CH*$_3$), 1.60 (s, 3H, =C*CH*$_3$), 2.03 (d, $^3J_{HH}$ = 6.2 Hz, 3H, CH*CH*$_3$), 2.08 (d, $^2J_{HH}$ = 14.0 Hz, 1H, CH*CH*$_2$), 2.51 (d, $^2J_{HH}$ = 14.0 Hz, 1H, CH*CH*$_2$), 2.80 (s, 3H, N*CH*$_3$), 2.90 (s, 3H, N*CH*$_3$), 2.95 (s, 1H, As*CH*), 3.21 (d, $^3J_{HH}$ = 9.2 Hz, 1H, *CH*CH_2), 3.80 (s, 1H, As*CH*), 4.44 (q, $^3J_{HH}$ = 6.2 Hz, 1H, *CH*CH_3), 6.87–8.04 (m, 21H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 14.1, 14.9, 25.3, 32.0, 35.3, 52.3, 52.7, 53.2, 54.9, 75.5, 123.9, 125.2, 125.7, 126.4, 127.6, 128.7, 128.9, 129.2, 129.3, 129.7, 130.2, 130.5, 130.6, 131.0, 131.6, 131.9, 132.1, 132.8, 133.0, 133.2, 133.4, 133.6, 133.9, 136.1, 136.8, 136.9, 151.9 152.2.

4.3. Removal of the chiral auxiliary: preparation of diiodo complex (−)-3

Complex (−)-**2** (0.29 g, 0.32 mmol) was dissolved in dichloromethane (50 mL) and treated with excess concentrated hydrochloric acid (2 mL) at room temperature for 5 min. The mixture was then washed with water (3 × 50 mL). Next, sodium iodide (0.1 g) in water (50 mL) was added and stirred vigorously for 3 min. The organic layer was washed with water (3 × 50 mL) and dried ($MgSO_4$). The solvent was removed and the complex (−)-**3** was isolated by column chromatography on a silica column with dichloromethane (0.19 g, 70%). $[\alpha]_D$ = −78.6 (*c* 0.14, CH_2Cl_2). Mp: 85–86 °C. Anal. Calcd for $C_{26}H_{26}As_2I_2Pd$: C, 36.8; H, 3.1. Found: C, 36.9; H, 3.2. ^{1}H NMR ($CDCl_3$, δ): 1.48 (s, 3H, =C*CH*$_3$), 1.57 (s, 3H, =C*CH*$_3$), 2.05 (dd, $^3J_{HH}$ = 9.5, $^2J_{HH}$ = 13.6 Hz, 1H, CH*CH*$_2$), 2.55 (d, $^2J_{HH}$ = 13.0 Hz, 1H, CH*CH*$_2$), 2.96 (dt, $^3J_{HH}$ = 2.1, $^3J_{HH}$ = 9.4 Hz, 1H, *CH*CH_2), 3.07 (d, $^3J_{HH}$ = 2.1 Hz, 1H, As*CH*), 3.52 (d, $^3J_{HH}$ = 2.6 Hz, 1H, As*CH*), 7.37–8.02 (m, 15H, aromatics). ^{13}C NMR ($CDCl_3$, δ): 14.3, 15.7, 30.5, 31.4, 52.2, 56.3, 128.6, 129.1, 129.8, 129.9, 130.0, 130.9, 131.0, 131.1, 131.3, 131.6, 133.3, 133.7, 134.3, 135.8.

4.4. Liberation of diarsine ligand (−)-4

A solution of (−)-**3** (0.10 g, 0.12 mmol) and potassium cyanide (1.0 g) in $CDCl_3$ (0.6 mL) and H_2O (0.1 mL) was shaken vigorously for 15 min. The organic layer was separated, washed with water (3 × 0.5 mL) and dried ($MgSO_4$). Upon removal of the solvent, the free ligand (−)-**4** was obtained as an air-sensitive solid in quantitative yield. $[\alpha]_D$ = −81.7 (*c* 6.16, $CDCl_3$). ^{1}H NMR ($CDCl_3$, δ): 1.43 (s, 3H, *CH*$_3$), 1.48 (d, 3H, *CH*$_3$), 2.02 (dt, $^3J_{HH}$ = 1.8, $^3J_{HH}$ = 11.4 Hz, 1H, Ph_2As*CH*), 2.42 (ddd, $^3J_{HH}$ = 2.3, $^2J_{HH}$ = 4.4, $^3J_{HH}$ = 13.3 Hz, 1H, CH*CH*$_2$), 2.65 (s, 1H, PhAs*CH*), 2.79 (dd, 1H, $^2J_{HH}$ = 4.7, $^3J_{HH}$ = 8.9 Hz, CH*CH*$_2$), 2.93 (s, 1H, PhAs*CH*), 7.23–7.60 (m, 15H, aromatics).

4.5. Preparation of complex 5

Complex (−)-**3** (0.09 g, 0.11 mmol) was dissolved in dichloromethane–diethyl ether and allowed to stand at room temperature for several days; deep red crystals of **5** were obtained (0.02 g, 22%). Mp: 174–175 °C. Anal. Calcd for $C_{48}H_{40}As_4I_4O_2Pd_2$: C, 34.5; H, 2.4. Found: C, 34.1; H, 2.6. ^{1}H NMR (CD_2Cl_2, δ): 7.34–7.79 (m, 5H, aromatics).

Table 1
Crystallographic data for complex **5**

	5
Formula	$C_{48}H_{40}As_4I_4O_2Pd_2$
Formula weight	1668.88
Space group	*P*1
Crystal system	Triclinic
a (Å)	10.0982(3)
b (Å)	10.6280(3)
c (Å)	12.4365(4)
α (°)	100.939(2)
β (°)	100.910(2)
γ (°)	97.918(2)
V (Å^3)	1265.74(7)
Z	1
T (K)	223(2)
D_{calcd} (g cm^{-3})	2.189
λ (Å)	0.71073
μ (mm^{-1})	5.780
F(000)	780
R_1 (obs data)[a]	0.0254
wR_2 (obs data)[b]	0.0616

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.
[b] $wR_2 = \sqrt{\{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}}$, $w^{-1} = \sigma^2(F_o)^2 + (aP)^2 + bP$.

Table 2
Selected bond lengths (Å) and angles (deg) for complex **5**

Pd(1)–As(1)	2.379(1)	Pd(1)–As(2)	2.379(1)
Pd(1)–I(1)	2.665(1)	Pd(1)–I(2)#1	2.743(1)
Pd(1)–I(2)	2.954(1)	Pd(1)–Pd(1)#1	2.966(1)
As(1)–O(1)	1.785(2)	As(1)–C(7)	1.931(3)
As(1)–C(1)	1.934(4)	As(2)–O(1)#1	1.783(2)
As(2)–C(19)	1.931(3)	As(2)–C(13)	1.938(3)
I(2)–Pd(1)#1	2.7431(3)	O(1)–As(2)#1	1.783(2)
As(1)–Pd(1)–As(2)	173.8(1)	As(1)–Pd(1)–I(1)	87.8(1)
As(2)–Pd(1)–I(1)	88.0(1)	As(1)–Pd(1)–I(2)#1	89.5(1)
As(2)–Pd(1)–I(2)#1	89.9(1)	I(1)–Pd(1)–I(2)#1	131.8(1)
As(1)–Pd(1)–I(2)	93.4(1)	As(2)–Pd(1)–I(2)	92.4(1)
I(1)–Pd(1)–I(2)	110.8(1)	I(2)#1–Pd(1)–I(2)	117.4(1)
As(1)–Pd(1)–Pd(1)#1	92.9(1)	As(2)–Pd(1)–Pd(1)#1	92.3(1)
I(1)–Pd(1)–Pd(1)#1	166.0(1)	I(2)#1–Pd(1)–Pd(1)#1	62.2(1)
I(2)–Pd(1)–Pd(1)#1	55.2(1)	O(1)–As(1)–C(7)	96.5(1)
O(1)–As(1)–C(1)	98.6(1)	C(7)–As(1)–C(1)	105.2(1)
O(1)–As(1)–Pd(1)	113.9(1)	C(7)–As(1)–Pd(1)	121.4(1)
C(1)–As(1)–Pd(1)	117.2(1)	O(1)#1–As(2)–C(19)	97.1(1)
O(1)#1–As(2)–C(13)	99.0(1)	C(19)–As(2)–C(13)	103.8(1)
O(1)#1–As(2)–Pd(1)	114.4(1)	C(19)–As(2)–Pd(1)	121.3(1)
C(13)–As(2)–Pd(1)	117.3(1)		

4.6. X-ray crystal structure determination of complex 5

Crystal data for complex **5** and a summary of the crystallographic analysis are given in Table 1. Diffraction data were collected on a Bruker X8 CCD diffractometer with Mo Kα radiation (graphite monochromator). SADABS absorption corrections were applied. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were introduced at calculated positions and refined riding on their carrier atoms. The absolute configuration of the chiral complex was determined unambiguously by using the Flack parameter. CCDC 996101 contained the supplementary crystallographic data for **5**. These data could be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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References

1. Ehrlich, P.; Bertheim, A. *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 756.
2. Christiansen, W. G. *J. Am. Chem. Soc.* **1921**, *43*, 2202.
3. Lloyd, N. C.; Morgan, H. W.; Nicholson, B. K.; Rouimus, R. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 941.
4. Farina, V.; Krishman, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
5. Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014.
6. van Vliet, M. C. A.; Arends, I. W. C. E.; Sheldon, R. A. *Tetrahedron Lett.* **1999**, *40*, 5239.
7. van der Veen, L. A.; Keeven, P. K.; Kamer, P. C.; van Leeuwen, P. W. N. M. *Chem. Commun.* **2000**, 333.
8. Ceccarelli, S.; Piarulli, U.; Gennari, C. *J. Org. Chem.* **2000**, *65*, 6254.
9. Baber, R. A.; Collad, S.; Hooper, M.; Orpen, A. G.; Pringle, P. G.; Willkinson, M. J.; Wingad, R. L. *Dalton Trans.* **2005**, *124*, 1491.
10. Wild, S. B. *Pure Appl. Chem.* **1990**, *62*, 1139.
11. Kojima, A.; Boden, C. D. J.; Shibasaki, M. *Tetrahedron Lett.* **1999**, *38*, 3459.
12. Doyle, R. J.; Habermehl, N.; Salem, G.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **2000**, 3603.
13. Coote, M. L.; Krenske, E. H.; Porter, K. A.; Weir, M. L.; Willis, A. C.; Zhou, X.; Wild, S. B. *Organometallics* **2008**, *27*, 5099.
14. Weir, M. L.; Cade, I. A.; Kilah, N. L.; Zhou, X.; Wild, S. B. *Inorg. Chem.* **2009**, *48*, 7482.
15. Lu, D.; Rae, A. D.; Salem, G.; Weir, M. L.; Willis, A. C.; Wild, S. B. *Organometallics* **2010**, *29*, 32.
16. Uberman, P. M.; Caira, M. R.; Martin, S. E. *Organometallics* **2013**, *32*, 3220.
17. Wild, S. B. *The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds*; Wiley: Chichester, U.K., 1994. p 110.
18. Wild, S. B. *Coord. Chem. Rev.* **1997**, *166*, 291.
19. Ma, M.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *Inorg. Chem.* **2007**, *46*, 9488.
20. Ma, M.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *J. Organomet. Chem.* **2008**, *693*, 3289.
21. Ma, M.; Pullarkat, S. A.; Yuan, M.; Zhang, N.; Li, Y.; Leung, P. H. *Organometallics* **2009**, *28*, 4886.
22. Ma, M.; Pullarkat, S. A.; Chen, K.; Li, Y.; Leung, P. H. *J. Organomet. Chem.* **2009**, *694*, 1929.
23. Ma, M.; Lu, R.; Pullarkat, S. A.; Deng, W.; Leung, P. H. *Dalton Trans.* **2010**, *39*, 5453.
24. Ma, M.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *Eur. J. Inorg. Chem.* **2010**, 1865.
25. Ma, M.; Yu, Z.; Zhu, L.; Pullarkat, S. A.; Leung, P. H. *J. Organomet. Chem.* **2014**, *756*, 34.
26. Chooi, S. Y. M.; Siah, S. Y.; Leung, P. H.; Mok, K. F. *Inorg. Chem.* **1993**, *32*, 4812.
27. Loh, S. K.; Mok, K. F.; Leung, P. H.; White, A. J. P.; Williams, D. J. *Tetrahedron: Asymmetry* **1996**, *7*, 45.