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(54) **THIOUREA COMPOSITIONS AND USES THEREOF**

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(73) Assignee: **The University of Hong Kong**, Hong Kong (CN)

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(21) Appl. No.: **11/089,197**

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(51) **Int. Cl.**
C07D 487/00 (2006.01)
C07D 403/02 (2006.01)

(52) **U.S. Cl.** **540/495**; 548/312.7

(58) **Field of Classification Search** 540/495; 548/312.7

See application file for complete search history.

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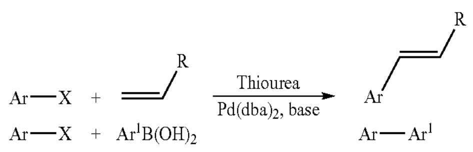
(57) **ABSTRACT**

The invention provides N,N'-disubstituted monothiourea or bis-thiourea-Pd(0) complexes that are useful as catalysts for palladium-catalyzed Heck reaction of aryl iodides and bromides with olefins, and as catalysts for palladium catalyzed Suzuki reactions of organoboric compounds and aryl halides.



8 Claims, 2 Drawing Sheets

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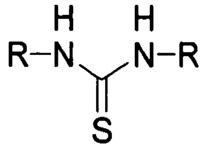
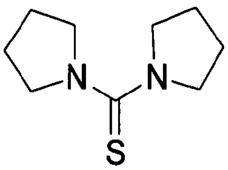
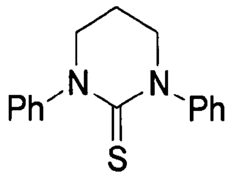
Figure 1



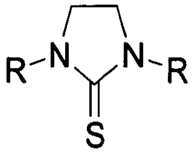
1a: R=H
1b: R=2,4,6-mesityl



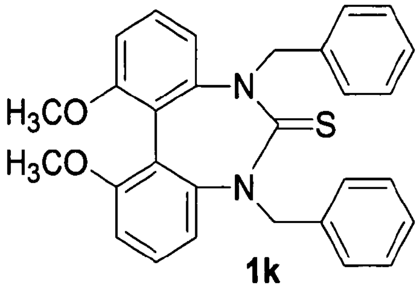
1c



1j

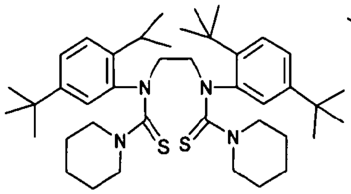


1d: R=H
1e: R=Me
1f: R=4-MeO-Ph
1g: R=Mesityl
1h: R=2,6-Et_2-Ph
1i: R=2,5-Bu^t_2-Ph

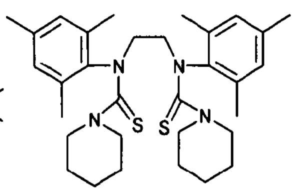


1k

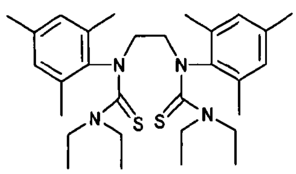
Figure 2



1l

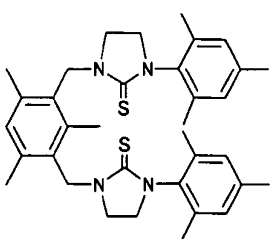


1m

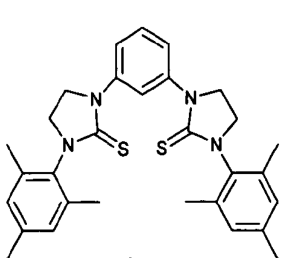


1n

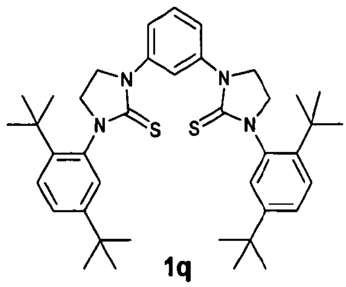
Figure 3



1o

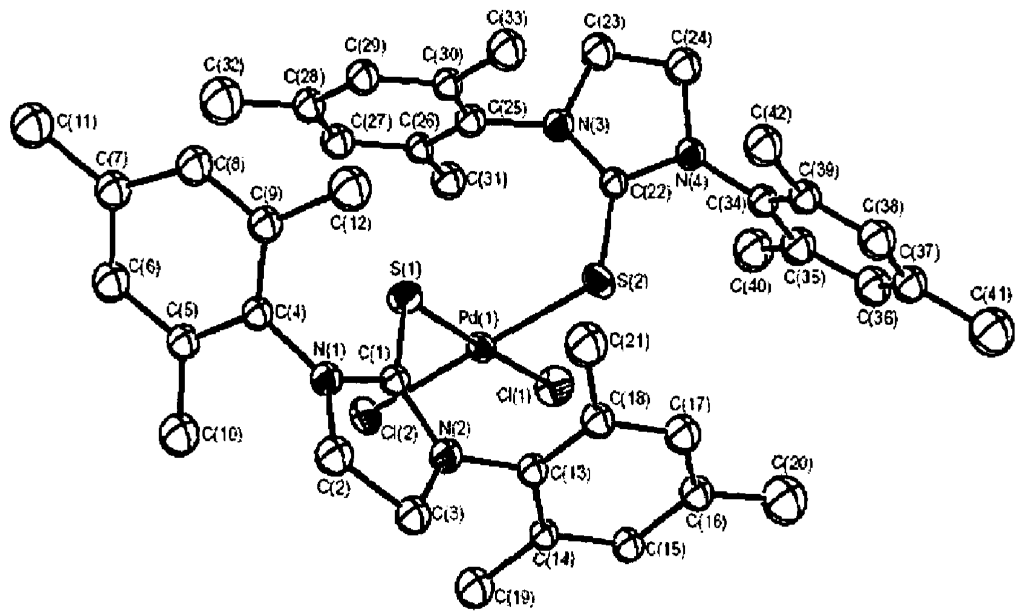


1p

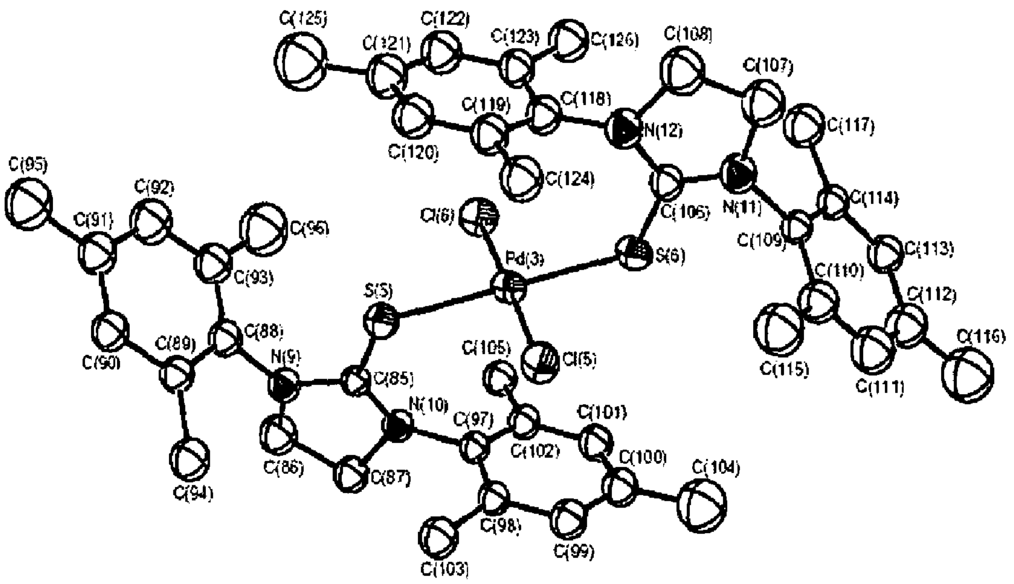


1q

Figure 4



Cis- $PdCl_2\cdot(1g)_2$



Trans- $PdCl_2\cdot(1g)_2$

THIOUREA COMPOSITIONS AND USES THEREOF

This application claims priority of provisional application U.S. Ser. No. 60/556,570, filed Mar. 26, 2004, the contents of which are being incorporated herein by reference.

FIELD OF THE INVENTION

This invention relates to thiourea ligands and more particularly to thiourea-palladium complexes useful as catalysts for palladium catalyzed arylation of alkenes in a chemical reaction known as the Heck reaction, and as catalysts for palladium catalyzed Suzuki reactions of organoboric compounds and aryl halides.

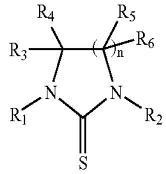
BACKGROUND OF THE INVENTION

The palladium catalyzed arylation of olefins (the Heck reaction) is one of the most versatile tools for C—C bond formation in organic synthesis.[1] Phosphine ligands are generally used to stabilize the reactive palladium intermediates, and excellent results have been reported for Pd-catalyzed Heck reactions when sterically bulky mono-phosphines, diphosphines, cyclometalated phosphines, or phosphites are used as the ligands.[2-5] The air-sensitivity of phosphine ligands, however, places significant limits on their synthetic applications. Therefore, the development of phosphine-free palladium catalysts is a topic of enormous interest.[6-8] Thioureas are air and moisture stable solids and have recently been, employed as ligands in Ru—, Rh—, or Pd-catalyzed reactions.[9-10] Very recently, Z. Yang[11] and coworkers reported the Heck and Suzuki reactions of highly active arenediazonium salts catalyzed by a chiral thiourea -Pd complex.

SUMMARY OF THE INVENTION

The invention provides thiourea-Pd(0) complexes that are air and moisture stable, highly active catalysts for the Heck reactions of aryl halides. More particularly, the invention provides the N,N'-disubstituted monothiourea ligand represented by generic structure I:

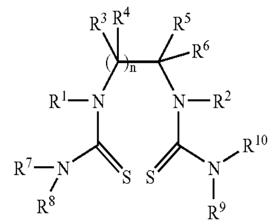
I



wherein n is an integer in the range of 1 to 8 inclusive; R_1 and R_2 are selected, independently for each occurrence, from the groups consisting of alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}; R_3, R_4, R_5, and R_6 are selected, independently for each occurrence, from the groups consisting of H, alkyl, halogenated alkyl, cycloalkyl, aryl, aralkyl, —$(CH_2)_m$—R_{80}, $COOR_v$ (where R_v=alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}), and $CONR_uR_v$ (where R_u or R_v=H, alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}); R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or polycycle; m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and the ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

The bis-thiourea ligand represented by generic structure II:

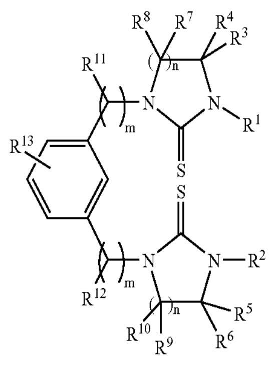
II



wherein n is an integer in the range of 1 to 8 inclusive; R_1 and R_2 are selected, independently for each occurrence, from the groups consisting of alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}; R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are selected, independently for each occurrence, from the groups consisting of H, alkyl, halogenated alkyl, cycloalkyl, aryl, aralkyl, —$(CH_2)_m$—R_{80}, $COOR_v$ (where R_v=alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}), and $CONR_uR_v$ (where R_u or R_v=H, alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}); R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or polycycle; m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and the ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

The bis-thiourea ligand represented by generic structure III:

III



wherein n is an integer in the range of 1 to 8 inclusive; R_1 and R_2 are selected, independently for each occurrence, from the groups consisting of alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}; R_3, R_4, R_5, R_6, R_3, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13} are selected, independently for each occurrence, from the groups consisting of H, alkyl, halogenated alkyl, cycloalkyl, aryl, aralkyl, —$(CH_2)_m$—R_{80}, $COOR_v$ (where R_v=alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}), and $CONR_uR_v$ (where R_u or R_v=H, alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}); R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or polycycle; m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and the ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows some representative structures of thiourea ligands I.

FIG. **2** shows some representative structures of thiourea ligands II.

FIG. **3** shows some representative structures of thiourea ligands III.

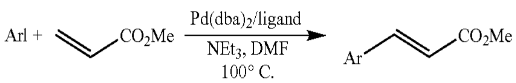
FIG. **4** shows structures of cis- and trans-$PdCl_2.(1g)_2$. (Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are shown at 30% probability).

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The invention provides acyclic and cyclic thioureas 1a-q (FIGS. **1**-**3**) and complexes thereof with Pd(0) or Pd(II) (FIG. **4**), which serve as catalysts for the Heck reaction between iodobenzene and methyl acrylate at 100° C. (Table 1).

TABLE 1

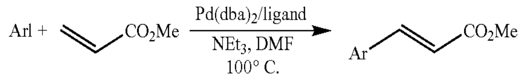
Screening thiourea ligands for the Pd-catalyzed Heck reaction of iodobenzene with methyl acrylate[a]



entry	ligand	Pd (mol %)	time (h)	yield[b]	TON
1	1e	0.1	1	>99	10^3
2	1g	0.01	2	>99	10^4
3	1h	0.01	2	>99	10^4
4	1i	0.01	1.5	>99	10^4
5	1l	0.01	6	86	8.6×10^3
6	1n	0.01	4	95	9.5×10^3
7	1o	0.01	4	45	4.5×10^3
8	1p	0.01	4	99	10^4
9	1q	0.01	2	99	10^4
10	1i	0.0001	48	50	5×10^5

TABLE 1-continued

Screening thiourea ligands for the Pd-catalyzed Heck reaction of iodobenzene with methyl acrylate[a]



entry	ligand	Pd (mol %)	time (h)	yield[b]	TON
11[c]	1n	0.001	0.5	99	10^5
12[d]	1q	0.0002	5	99	5×10^5
13[d]	1n	0.0001	12	99	10^6

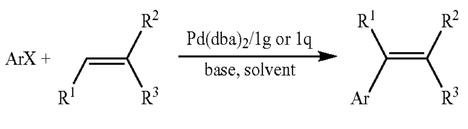
[a]Reactions were conducted under aerobic conditions.
[b]Yield was determined by ^1H NMR spectroscopy using nitrobenzene as the internal standard.
[c]At 150° C.
[d]At 180° C. under solvent-free condition

The reactions were conducted in air and that all the reagents were used directly as received. The structure of each thiourea ligand has a great influence on the catalytic efficacy of its palladium complex. Acyclic thioureas 1a-c were almost completely inactive, as was also the case for the cyclic thiourea 1d featuring an NH moiety. Good activity was observed, however, when using the N,N'-disubstituted bulky thioureas 1e-1q of different ring sizes as the ligands (Table 1 entries 1-8); the catalyst loading could be lowered down to 0.0001 mol %. The reaction also could be conducted at high temperature under solvent-free conditions without affecting the catalytic efficacy (entries 12 and 13).

The catalytic efficacy of the thiourea 1g-Pd(0) and 1q-Pd (0) complex in the Heck reaction was studied further with a number of aryl halides and olefins at 100-130° C. Table 2 indicates that high yields were obtained using 0.01 mol % Pd catalyst for olefins such as butyl acrylates (entries 1-2), Olefins that are α- or β-subsituted are also suitable substrates and give trisubstituted olefins,[12] but higher catalyst loadings and reaction temperatures were required (entries 3-4). In general, higher catalyst loadings and temperatures were required to force the completion of the reactions of the aryl bromides compared to the case of aryl iodides (entries 5-8). 3-Bromopyridine was also efficiently coupled with styrene in 90% yield in the presence of 0.1 mol % of Pd (entry 9). The deactivated bromide could be coupled at higher temperature (entry 10, 160° C.).

TABLE 2

Heck reaction of aryl iodides and bromides with olefins[a]



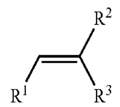
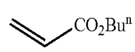
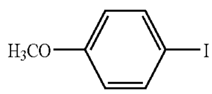
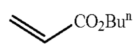
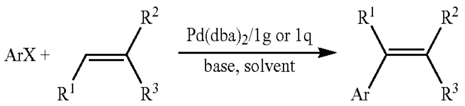
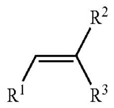
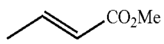
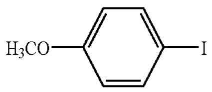
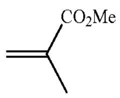
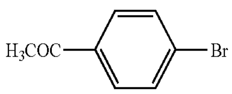
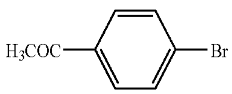
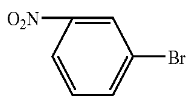
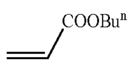
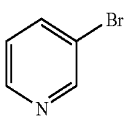
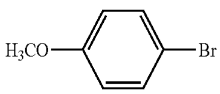
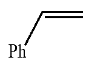
entry	ligand	ArI		Pd (mol %)	time (h)	yield (%)[b]
1	1g	PhI		0.01	2	99
2	1q			0.01	3	99

TABLE 2-continued

Heck reaction of aryl iodides and bromides with olefins[a]

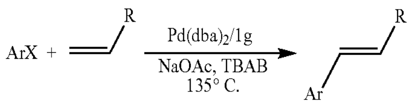


entry	ligand	ArI		Pd (mol %)	time (h)	yield (%)[b]
3	1g	PhI		1	10	88
4	1q			0.5	5	68
5	1g		COOMe	0.1	15	92
6	1g		Ph	0.1	15	99
7	1g	PhBr	Ph	0.1	24	74
8	1q			0.1	10	99
9	1g		Ph	0.1	24	90
10	1q			0.5	24	76

Beller[13] reported that the Heck reactions of aryl chlorides could be greatly improved when using Bu_4NBr as an ionic liquid solvent.[14] In fact, this system is also suitable for the thiourea 1g-Pd(0)-catalyzed Heck reactions of deactivated bromides and activated chlorides, when the reaction temperature is elevated slightly. The results were summarized in Table 3. Excellent yields were achieved for deactivated bromides after their reaction for 24 h in the presence of 0.5 mol % of Pd (entries 1-3), but incomplete conversion occurred when using 0.2 mol % Pd catalyst (entry 4). Under the same conditions, activated aryl chlorides were coupled successfully with styrene within 24 h when using 1 mol % of the Pd catalyst (entries 5-7). n-Butyl acrylate displayed reactivity that was slightly lower than that of styrene, but good yields were also obtained (entries 8-10). Chorobenzene itself, however, was completely inert, even when we used a higher loading of the Pd catalyst (2 mol %) (entry 11).

TABLE 3

Heck reactions of deactivated bromides and activated chlorides with olefins



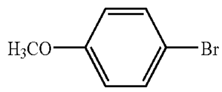
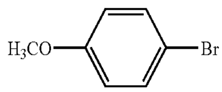
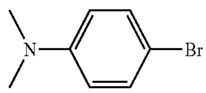
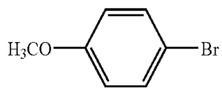
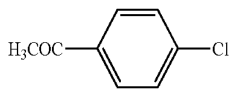
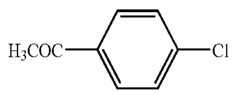
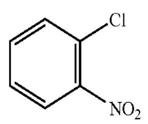
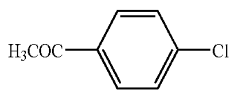
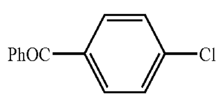
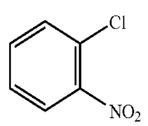
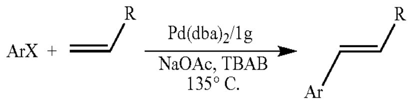
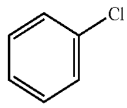
entry	ArX	R	Pd (mol %)	time (h)	yield (%)[b]
1		Ph	0.5	24	99
2		COO^{n}Bu	0.5	24	99
3		COO^{n}Bu	0.5	24	97
4		Ph	0.2	30	80
5		Ph	1	24	96
6		Ph	0.5	30	67
7		Ph	1	24	99
8		COO^{n}Bu	2	24	77
9		COO^{n}Bu	1	24	80
10		COO^{n}Bu	1	24	90

TABLE 3-continued

Heck reactions of deactivated bromides and activated chlorides with olefins



entry	ArX	R	Pd (mol %)	time (h)	yield (%)[b]
11		Ph	2	24	<5

The Pd-catalysed Suzuki cross-coupling reaction of aryl halides with aryl boric acids provides a general and efficient synthetic route to biaryl compounds and has found wide application in many areas of organic synthesis.[15] The operationally simple and air-stable catalytic system of thiourea-Pd catalyst inspired us to investigate its scope in Suzuki reaction. As revealed in Table 4 using 1q as the ligand, for p-iodoanisole, excellent isolated yield was obtained at a loading of 0.01 mol % Pd at 100° C. after 3h under aerobic conditions (Table 3, entry 1).

Encouraged by the result, we began to evaluate the coupling reaction of aryl bromides with aryl boric acids. For activated bromides, almost quantitative yields were achieved within 3h in the presence of 0.1 mol % Pd under the same conditions (entries 2-6). On the other hand, low yield was obtained when deactivated p-bromoanisole was applied at 0.5 mol % Pd at 120° C. (entry 7), and similar results were gained when a bulky monodentate 1i was used (entry 8). However, the yield could be increased adding 20 mol % TBAB (entry 9). For 3,5-difluorophenylboric acid, better result could be obtained when the reaction was conducted in neat TBAB (entry 10). Acceptable yield was achieved for p-nitrochlorobenzene at 1 mol % Pd adding 20 mol % TBAB (entry 11 vs 12). Notably 1-bromostyrene also displayed high reactivity to phenylboric acid in thiourea-Pd system (entry 13). Moreover, potassium aryl trifluoroborates[16] have been found to be more reactive than the corresponding organoboric acid, and high yields were obtained at only 0.1 mol % Pd at 100° C. (entries 14 and 15). We also conducted the Suzuki reaction at further decreased catalyst loading (0.01 mol %), and quantitative yield was obtained for 3-nitro-bromobenzene at 120° C. in 3h (entry 16).

TABLE 4

Suzuki coupling reaction catalyzed by 1q-Pd(dba)$_2$

$$\mathrm{ArX} + \mathrm{Ar^1B(OH)_2} \xrightarrow[\mathrm{K_2CO_3,\ NMP,\ H_2O}]{\mathrm{Pd(bda)_2\text{-}1q}} \mathrm{Ar{-}Ar^1}$$

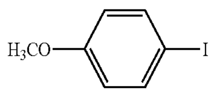
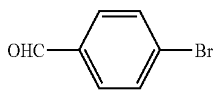
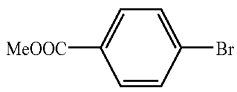
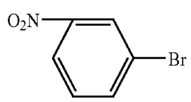
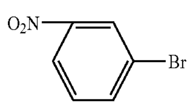
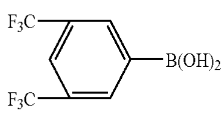
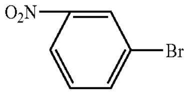
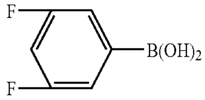
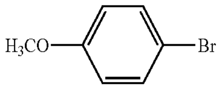
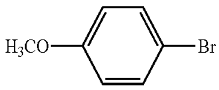
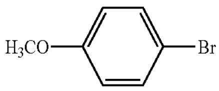
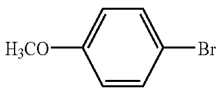
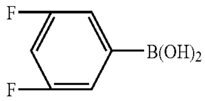
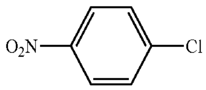
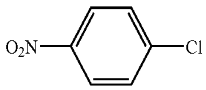
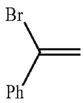
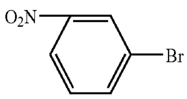
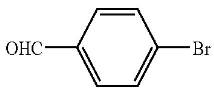
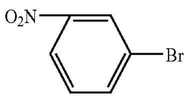
Entry	Ar^1X	$Ar^2B(OH)_2$	Pd (mol %)	T (° C.)	t (h)	Yield (%)
1		$PhB(OH)_2$	0.01	100	3	92
2		$PhB(OH)_2$	0.1	100	3	92[c]
3		$PhB(OH)_2$	0.1	100	3	90
4		$PhB(OH)_2$	0.1	100	3	99
5			0.1	100	2	97

TABLE 4-continued

Suzuki coupling reaction catalyzed by 1q-Pd(dba)$_2$

$$ArX + Ar^1B(OH)_2 \xrightarrow[K_2CO_3,\ NMP,\ H_2O]{Pd(bda)_2\text{-}1q} Ar—Ar^1$$

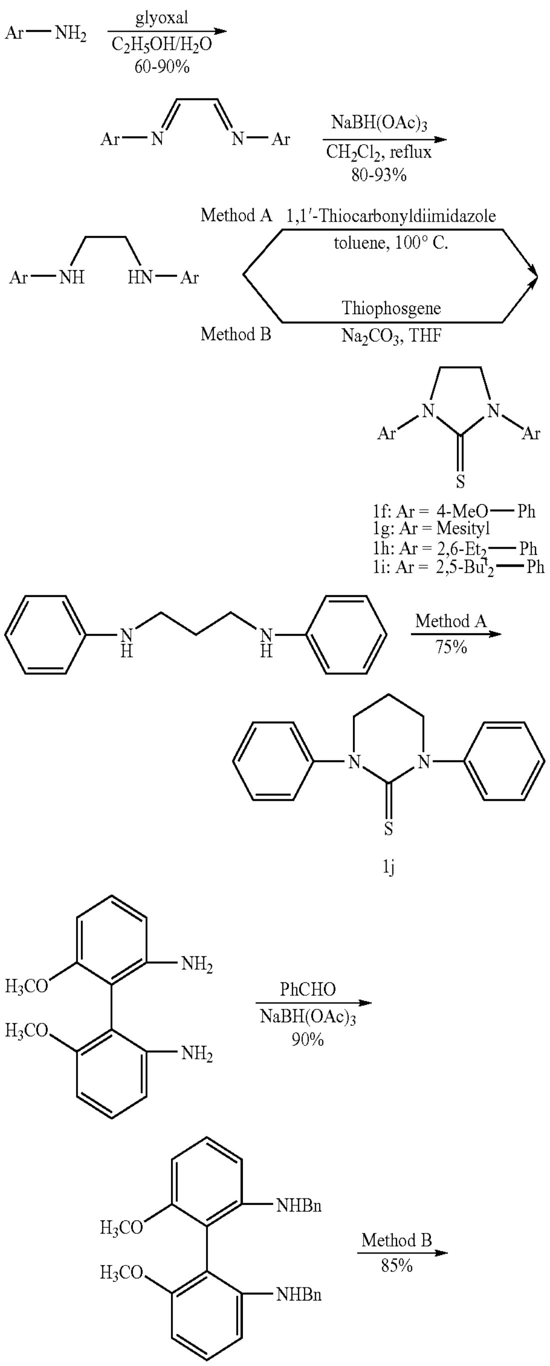
Entry	Ar^1X	$Ar^2B(OH)_2$	Pd (mol %)	T (° C.)	t (h)	Yield (%)
6			0.1	100	2	99
7		$PhB(OH)_2$	0.5	120	10	33
8[c]		$PhB(OH)_2$	0.5	120	10	27
9[d]		$PhB(OH)_2$	0.5	120	12	67
10[e]			0.5	130	12	51
11[f]		$PhB(OH)_2$	1	130	40	10
12[d,f]		$PhB(OH)_2$	1	130	24	49
13		$PhB(OH)_2$	0.1	100	1	80
14		$PhBF_3K$	0.1	100	1	99
15		$PhBF_3K$	0.1	100	1.5	87
16		$PhB(OH)_2$	0.01	120	3	99

In conclusion, the palladium complexes of cyclic and acyclic thiourea demonstrated high thermal stability and excellent catalytic activity in Heck and Suzuki coupling reactions under aerobic conditions. Remarkable TONs and TOFs were achieved in the coupling reactions (TONs up to 1,000,000, TOFs up to 200,000, for the reaction of PhI and n-butyl acrylate).

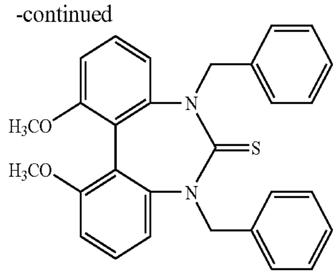
EXAMPLE 1

Synthesis of Cyclic Thioureas 1f-1k

Scheme 1



-continued



1k

Two methods were used for the synthesis of cyclic thiourea ligands (Scheme 1)

Method A:

To a N,N'-diaryl diamine solution in dry toluene was added 1,1'-thiocarbonyl diimidazole (1.2 equiv). Then the solution was stirred at 100° C. and the reaction was monitored by TLC. After completion, the solution was diluted with ethyl acetate and washed with dilute HCl and brine. The organic layer was concentrated under vacuum. The pure thiourea was obtained through flash chromatography or recrystallization from 95% ethanol.

Method B:

To a stirred mixture of N,N'-diaryl diamine and Na_2CO_3 (1.5 equiv) in dry THF was added a solution of thiophosgene (1.2 equiv) in THF dropwise at room temperature. After stirring at room temperature overnight, water and ethyl acetate were added. The organic layer was washed with dilute HCl and brine, dried and concentrated. The pure thiourea was obtained through flash chromatography or recrystallization from 95% ethanol.

Preparation of 1f:

Using method A; 75% yield. M.p. 167-168° C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J=9.0 Hz, 4H), 6.95 (d, J=9.0 Hz, 4H), 4.08 (s, 4H), 3.81 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.2, 158.1, 138.8, 127.5, 114.2, 55.4, 49.8; IR (cm^{-1}): 1511, 1443, 1285; LRMS (EI): 314 (M^+, 100); HRMS (EI): calcd for $C_{17}H_{18}N_2O_2S$ (M^+) 314.1089, found 314.1088.

Preparation of 1g:

Using method B; 85% yield. M.p. 218-218.5° C.; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (s, 4H), 3.94 (s, 4H), 2.26 (s, 6H), 2.24 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 138.2, 136.6, 134.5, 129.5, 47.6, 21.1, 17.8; IR (cm^{-1}): 1488, 1331, 1271; LRMS (FAB): 339 (M^++1, 100); HRMS (FAB): calcd for $C_{21}H_{26}N_2S$ (M^++1) 339.1894, found 339.1879.

Preparation of 1h:

Using method B; 70% yield. M.p. 152-153° C.; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (t, J=6.6 Hz, 2H), 7.20 (d, J=7.5 Hz, 4H), 4.02 (s, 4H), 2.80-2.70 (m, 4H), 2.69-2.60 (m, 4H), 1.33 (t, J=7.5 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.6, 142.5, 136.1, 128.8, 126.5, 49.1, 24.0, 14.4; IR (cm^{-1}): 1484, 1285; LRMS (EI): 366 (M^+, 39), 337 (100); HRMS (EI): calcd for $C_{23}H_{30}N_2S$ (M^+) 366.2130, found 366.2120.

Preparation of 1i:

Diimine: 92% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (s, 2H), 7.35 (d, J=8.3 Hz, 2H), 7.25 (d, J=8.3 Hz, 2H), 6.86 (s, 2H), 1.43 (s, 18H), 1.34 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 150.1, 150.0, 140.4, 126.0, 123.8, 116.0, 35.3, 34.4, 31.3, 30.5; IR (cm^{-1}): 1609, 1492, 1265; LRMS (EI): 432 (M^+, 100); HRMS (EI): calcd for $C_{30}H_{44}N_2$ (M^+) 432.3504, found 432.3504.

Diamine: 90% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J=6.1 Hz, 2H), 6.80 (s, 2H), 6.75 (d, J=6.1 Hz, 2H), 4.18 (br s, 2H, NH), 3.57 (s, 4H), 1.39 (s, 18H), 1.32 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 146.2, 131.2, 126.0, 114.6, 110.0, 45.0, 34.4, 33.8, 31.4, 30.2; IR (cm^{-1}): 3688, 3601, 1561, 1265; LRMS (EI): 436 (M^+, 20), 219 (100); HRMS (EI): calcd for $C_{30}H_{48}N_2$(M^+) 436.3817, found 436.3817.

Thiourea Ii was prepared using method B. A solution of Thiophosgene in dilute THF must be dropped very slowly. 1i was isolated as a white solid (75% yield) after flash chromatography on silica gel. M.p. 212-214° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J=8.5 Hz, 2H), 7.32 (d, J=8.5 Hz, 2H), 7.02 (s, 2H), 4.06-4.03 (m, 2H), 3.93-3.91 (m, 2H), 1.50 (s, 18H), 1.30 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.5, 150.4, 145.0, 140.8, 128.0, 127.8, 125.3, 53.4, 35.4, 34.3, 32.1, 31.3; IR (cm^{-1}): 1418, 1275; LRMS (FAB): 479 (M^++H); FAB-HRMS: calcd for $C_{31}H_{46}N_2S$ (M^++H) 479.3460, found 479.3460.

Preparation of 1j:

Using method A, 75% yield. M.p. 173-174° C.; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.15 (m, 10H), 3.82-3.77 (m, 4H), 2.32-2.24 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.7, 147.4, 129.2, 127.4, 125.8, 51.4, 22.3; IR (cm^{-1}): 1494, 1285; LRMS (EI): 268 (M^+, 73); EI-HRMS: calcd for $C_{16}H_{16}N_2S$ (M^+) 268.1034, found 268.1015.

Preparation of 1k:

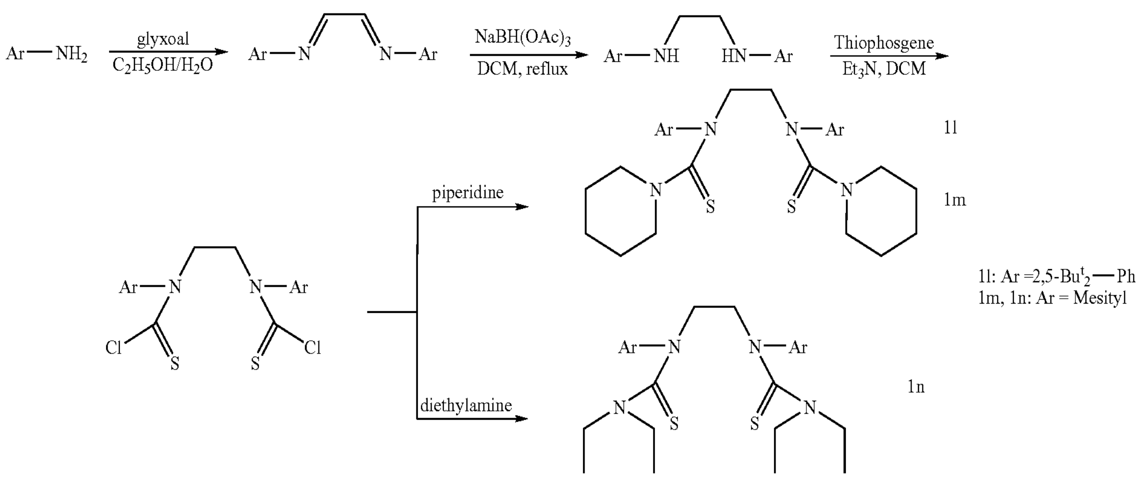
To a stirred suspension of racemic 2,2'-diamino-6,6'-dimethoxybiphenyl[2] (60 mg, 0.25 mmol) and $NaBH(OAc)_3$ (212 mg, 1 mmol) in dichloromethane (10 mL) was added a solution of benzaldehyde (0.06 ml, 0.58 mmol) in dichloromethane (2 mL) dropwise at room temperature. Then the mixture was stirred overnight. Flash chromatography on silica gel gave N,N'-dibenzyl diamine as a white solid (94 mg, 90%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.26-7.11 (m, 12H), 6.38 (d, J=8.2 Hz, 2H), 6.32 (d, J=7.7 Hz, 2H), 4.32 (s, 4H), 4.17 (br s 2H), 3.70 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 147.3, 139.9, 129.6, 128.4, 126.7, 126.6, 107.2, 104.2, 100.6, 55.7, 47.5; IR (cm^{-1}): 3432, 3086, 3051, 2938, 1586, 1496, 1472, 1422, 1282, 1131; LRMS (EI): 424 (M^+, 33), 333 (100); HRMS (EI): calcd for $C_{28}H_{28}N_2O_2S$ (M^+) 424.2151, found 424.2138.

Thiourea 1k was prepared using method B, 85% yield. M.p. 179-180° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (t, J=8.2 Hz, 2H), 7.04-7.00 (m, 6H), 6.88 (d, J=8.2 Hz, 2H), 6.83-6.80 (m, 6H), 5.72 (d, J=15.3 Hz, 2H), 4.81 (d, J=15.3 Hz, 2H), 3.75 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.6, 157.2, 147.7, 137.1, 128.7, 127.9, 127.5, 126.7, 121.8, 113.9, 108.8, 56.8, 55.9; IR (cm^{-1}): 3051, 1592, 1579, 1464, 1420, 1245, 1190; LRMS (EI): 466 (M^+, 100), 375 (86); HRMS (EI): calcd for $C_{29}H_{26}N_2O_2S$ (M^+) 466.1715, found 466.1718.

EXAMPLE 2

Synthesis of Acyclic Bis-Thiourea Ligands

Scheme 2



A solution of N,N'-diaryl diamine (1.0 mmol) and NEt_3 (3 equiv) in THF was dropped to a stirred solution of thiophosgene (3.0 equiv) in dry THF at 0° C. After stirred at room temperature overnight, the organic layer was washed with water, dried and concentrated.

For the synthesis of acyclic bis-thiourea, the dichloride obtained above and excess secondary amine were heated at 100° C. in a sealed pressure tube for 24 hours. Then the solution was diluted with EtOAc and washed with dilute HCl and brine. The organic layer was dried and concentrated. Flash chromatography gave the pure bis-thiourea as a white solid.

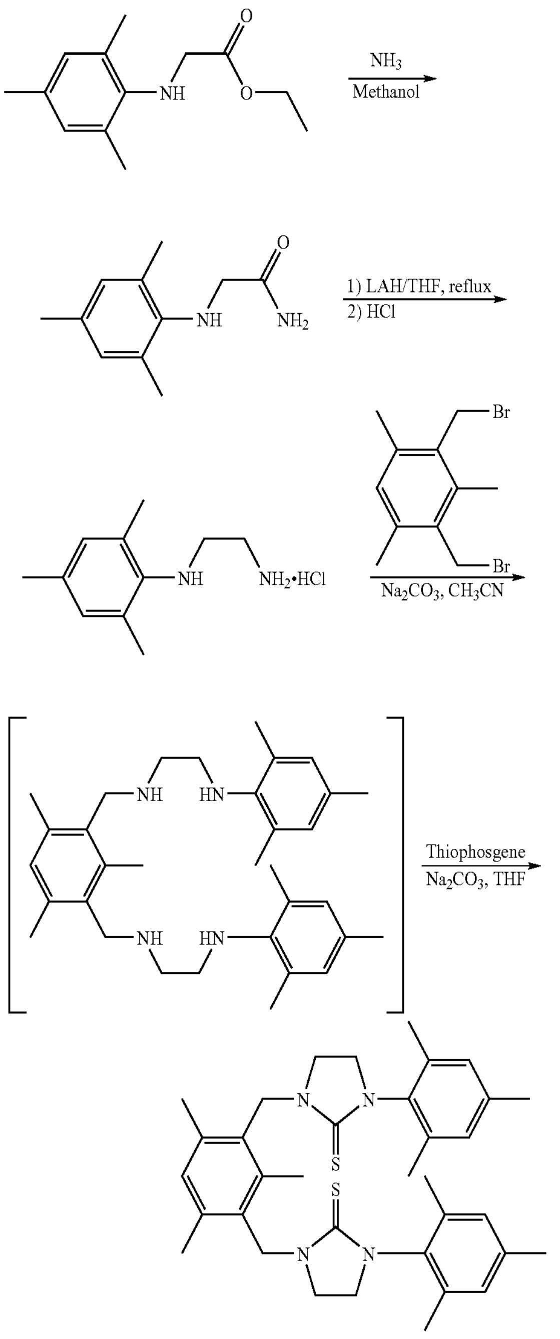
1l: White solid, 95% yield; m.p 225-226° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 2H), 7.21-7.18 (m, 2H), 7.18-7.00 (m, 2H), 4.87-4.79 (m, 2H), 4.15-4.11 (m, 2H), 3.54-3.35 (m, 8H), 1.44-1.19 (m, 48H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0, 149.1, 142.9, 141.3, 129.8, 127.4, 124.1, 54.0, 52.5, 35.6, 34.0, 32.0, 31.1, 25.2, 24.2; IR (cm^{-1}): 2958, 2865, 1609, 1440, 1397, 1362, 1244, 1185, 1133, 1026; ESI LRMS: 690(M, 2), 359(100); EI HRMS: calcd for $C_{42}H_{66}N_4S_2$ 690.4729, found 690.4717.

1m: White solid, 40% yield for two steps; m.p 222-224° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 4H), 4.29 (s, 4H), 3.30-3.27 (m, 8H), 2.25 (s, 6H), 2.18 (s, 12H), 1.39-1.36 (m, 4H), 1.17-1.15 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 141.3, 136.1, 134.3, 130.0, 51.9, 50.9, 25.2, 24.2, 20.7, 19.1; IR (cm^{-1}): 2934, 2851, 1609, 1473, 1422, 1369, 1245, 1185, 1159, 1131, 1027; EI LRMS: 550 (M, 34), 152 (100); EI HRMS: calcd for $C_{32}H_{46}N_4S_2$ 550.3164, found 550.3158.

1n: White solid, 38% yield for two steps; m.p 197-199° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 4H), 4.29 (s, 4H), 3.30 (q, J=6.8 Hz, 8H), 2.24 (s, 6H), 2.21 (s, 12H), 0.73 (t, J=6.8 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 141.6, 136.4, 135.0, 51.3, 46.0, 20.8, 19.2, 11.7; IR (cm^{-1}): 2963, 2929, 1651, 1486, 1441, 1411, 1370, 1348, 1274, 1223, 1185, 1152, 1120, 1081, 1013; EI LRMS: 526 (M, 42), 277 (100); EI HRMS: calcd for $C_{30}H_{46}N_4S_2$ 526.3164, found 526.3168.

EXAMPLE 3

Synthesis of Cyclic Bis-Thiourea Ligand 1o



1o

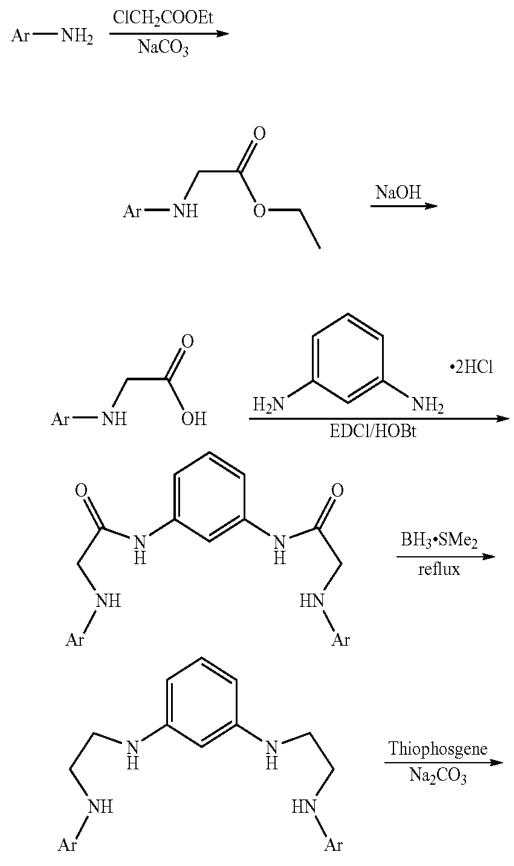
Preparation of 1o:

To a stirred mixture of diamine salt (2.0g, 9.2 mmol) and Na_2CO_3 (0.85g, 8 mmol) in CH_3CN (15 ml) was added slowly a solution of Bis(bromomethy) mesitylene (0.72g, 2.3 mmol) in CH_3CN (10 ml) at 81° C. The resulting mixture was refluxed for 24h. Then the mixture was diluted with ethyl acetate and washed with brine, dried and concentrated. The resulting oil was dissolved in THF (30 ml) and Na_2CO_3 (1.27g, 12 mmol) was added. Thiophosgene (0.7 ml, 9 mmol) in THF (10 ml) was dropped very slowly at room temperature. After stirred overnight, THF was removed, and water (20 ml) and ethyl acetate (40 ml) were added. The organic layer was washed with dilute HCl and brine, dried and concentrated. The pure bis-thiourea 1o was obtained through flash chromatography (20% ethyl acetate/petroleum ether) as a white solid (150 mg, 11%).

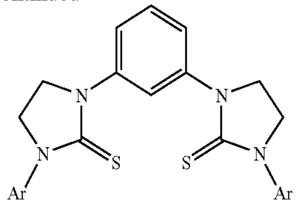
1o: m.p>230° C.; ^1H NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.95 (s, 4H), 4.97 (s, 4H), 3.66 (t, J=8.4 Hz, 4H), 3.41 (t, J=8.4 Hz, 4H), 2.43 (s, 3H), 2.40 (s, 6H), 2.29 (s, 6H), 2.22 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.7, 138.6, 138.1, 137.8, 136.5, 134.7, 130.8, 130.7, 129.4, 46.9, 46.3, 45.5, 21.0, 20.4, 17.7, 16.2; IR (cm^{-1}): 2917, 1609, 1489, 1437, 1408, 1326, 1309, 1273, 1233, 1033; ESI LRMS: 585 (M+1, 100); ESI HRMS: calcd for $C_{35}H_{44}N_4S_2$+Na 607.2905, found 607.2883.

EXAMPLE 4

Synthesis of Cyclic Bis-Thiourea Ligands 1p and 1q



-continued



1p: Ar = Mesityl
1q: Ar = 2,5-Bu^t_2—Ph

Preparation of 1p and 1q:

Borane-dimethylsulfide (2M in THF) (3.6 ml 7.2 mmol, 8equiv.) was added to a solution of diamide (0.9 mmol) in THF (20 ml) at 0° C. Then the solution was refluxed overnight. After cooling to room temperature, methanol was added very slowly to destroy the excess borane. The solvent was removed. Methanol (10 ml) was added and removed again under reduced pressure. The resulting tetraamine was directly used in the next step.

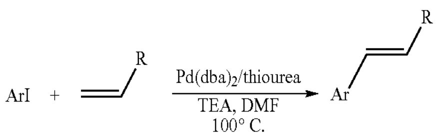
To a stirred mixture of tetraamine obtained above and Na_2CO_3 (6 equiv.) in dry THF was added a dilute solution of thiophosgene in THF. Then the mixture was stirred at room temperature overnight. The pure cyclic bis-thiourea was obtained as a white solid through flash chromatography and recrystalyzation from ethanol.

1p: White solid, 45% yield for two steps; m.p>230° C.; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.51-7.44 (m, 3H), 6.97 (s, 4H), 4.29 (t, J=8.4 Hz, 4H), 3.91 (t, J=8.4 Hz, 4H), 2.31 (s, 6H), 2.28 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 141.0, 138.3, 136.3, 134.7, 129.4, 128.6, 121.1, 120.2, 49.3, 47.2, 21.0, 17.8; IR (cm^{-1}): 2917, 1604, 1489, 1421, 1306, 1277, 1076; ESI LRMS: 515 (M+1, 100); ESI HRMS: calcd for $C_{30}H_{34}N_4O_4S_2$+H 515.2303, found 515.2294.

1q: White solid, 41% yield for two steps; m.p>2300C; ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.24-8.22 (m, 1H), 7.53-7.43 (m, 3H), 7.38 (d, J=2.0 Hz, 2H), 7.35 (d, J=2.0 Hz, 2H), 7.11 (s, 2H), 4.29-4.18 (m, 4H), 4.13-4.07 (m, 2H), 4.01-3.93 (m, 2H), 1.48 (s, 18H), 1.34 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.1, 150.5, 145.0, 141.2, 139.6, 128.8, 128.7, 128.2, 127.5, 125.5, 121.8, 121.6, 121.2, 52.6, 49.4, 35.4, 34.3, 31.9, 31.2; IR (cm^{-1}): 2960, 1604, 1559, 1475, 1414, 1297, 1084; ESI LRMS: 655 (M+1, 37), 639 (100); ESI HRMS: calcd for $C_{40}H_{54}N_4S_2$+H 655.3868, found 655.3864

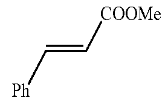
EXAMPLE 5

General Procedure for Heck Reaction of Aryl Iodides and Olefins

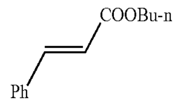


$Pd(dba)_2$ (1.5 mg, 0.0025 mmol) and thiourea (4 equiv) were stirred in DMF (0.5 mL) for 0.5 h at rt. Iodobenzene (0.28 mL, 2.5 mmol, substrate/catalyst ratio=1000:1) and methyl acrylate (0.27 mL, 3.0 mmol) and TEA (0.42 mL, 3.0

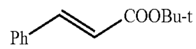
mmol) were then added. The flask was sealed with rubber septa and heated at 100° C. (the same result was obtained when the reaction was conducted with a condenser in open air). After the indicated time, the solution was diluted with ethyl acetate (20 mL) and washed with water and brine. Ethyl acetate was removed under vacuum and nitrobenzene (0.128 mL) was added as an internal standard. The yield of coupling product was determined by ^{1}H NMR (400 MHz or 300 MHz) analysis, by comparing the peak intensities of the α/β-H of the product and the ortho-H of nitrobenzene (internal standard).



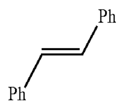
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.63 (m, 2H), 7.54 (d, J=4.1 Hz, 2H), 7.38 (d, J=3.3 Hz, 1H), 7.10 (t, J=6.5 Hz, 1H), 6.44 (d, J=16.1 Hz, 1H), 3.81 (s, 3H). To determine the reaction yield, the product peak at 6.44 ppm was selected for comparison with that of the ortho-H (at 8.20 ppm) of nitrobenzene (internal standard).



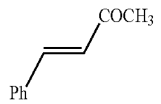
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J=16.0 Hz, 1H), 7.52-7.57 (m, 2H), 7.40-7.45 (m, 3H), 6.49 (d, J=16.0 Hz, 1H), 4.26 (t, J=6.9 Hz, 2H), 1.71-1.78 (m, 2H), 1.54-1.45 (m, 2H), 1.00 (t, J=7.4 Hz, 3H).



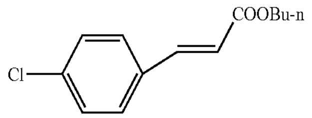
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J=16.0 Hz, 1H), 7.53-7.57 (m, 2H), 7.40-7.45 (m, 3H), 6.49 (d, J=16.0 Hz, 1H), 1.34 (s, 9H).



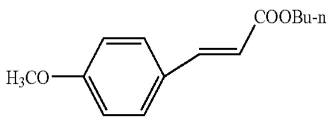
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J=7.2 Hz, 4H), 7.38 (dd, J=7.1, 1.5 Hz, 4H), 7.28 (d, J=7.2 Hz, 2H), 7.13 (s, 2H).



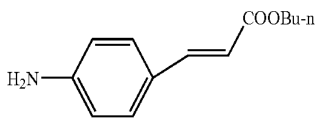
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J=9.4 Hz, 2H), 7.52 (d, J=16.0 Hz, 1H), 7.40 (t, J=3.5 Hz, 3H), 6.72 (d, J=16.0 Hz, 1H), 2.39 (s, 3H).



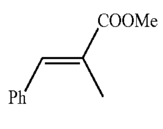
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J=16.2 Hz, 1H), 7.43 (d, J=6.2 Hz, 2H), 7.35 (d, J=6.2 Hz, 2H), 6.40 (d, J=16.2 Hz, 1H), 4.26 (t, J=6.9 Hz, 2H), 1.781.71 (m, 2H), 1.541.45 (m, 2H), 1.00 (t, J=7.4 Hz, 3H).



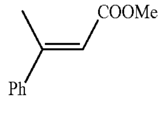
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J=16.0 Hz, 1H), 7.51 (d, J=8.9 Hz, 2H), 6.94 (d, J=8.9 Hz, 2H), 6.36 (d, J=16.0 Hz, 1H), 4.25 (t, J=6.8 Hz, 2H), 3.87 (s, 3H), 1.76-1.70 (m, 2H), 1.52-1.46 (m, 2H), 1.02 (t, J=7.5 Hz, 3H).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J=8.4 Hz, 2H), 7.56 (d, J=15.7 Hz, 1H), 6.62 (d, J=8.4 Hz, 2H), 6.51 (d, J=15.7 Hz, 1H), 6.17 (s, 2H), 4.26 (t, J=6.9 Hz, 2H), 1.781.77 (m, 2H), 1.54-1.45 (m, 2H), 1.00(t, J=7.4 Hz, 3H).



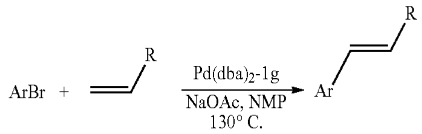
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J=6.9 Hz, 2H), 7.40-7.19 (m, 4H), 3.82 (s, 3H), 2.13 (s, 3H).



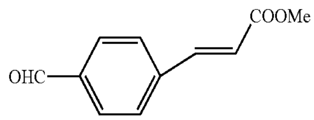
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.45 (m, 3H), 7.37-7.35 (m, 2H), 6.13 (q, J=1.2 Hz, 1H), 3.75 (s, 3H), 2.58 (d, J=1.3 Hz, 3H).

EXAMPLE 6

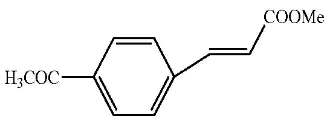
General Procedure for Heck Reaction of Aryl Bromides and Olefins



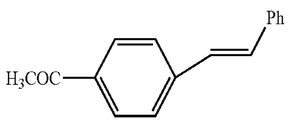
$Pd(dba)_2$ (1.5 mg, 0.0025 mmol) and thiourea 1g (3.4 mg, 0.01 mmol) were stirred in NMP (0.5 mL) for 0.5 h at rt. Aryl bromide (2.5 mmol, S/C=1000), olefin (3.8 mmol) and sodium acetate 330 mg (3.8 mmol) were added in turn. Then the flask was sealed with a septa and heated at 130° C. After indicated time, the solution was dilute with ethyl acetate (20 mL) and washed with water and brine. Ethyl acetate was removed under vacuum and nitrobenzene (0.128 mL) was added as internal standard. The yield of coupling product was determined by ^{1}H NMR (400 MHz or 300 MHz) analysis, by comparing the peak intensities of the cc/P—H of the product and the ortho-H of nitrobenzene (internal standard).



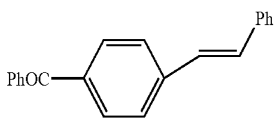
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.87 (d, J=8.1 Hz, 2H), 7.70-7.62 (m, 3H), 6.52 (d, J=15.9 Hz, 1H), 3.79 (s, 3H).



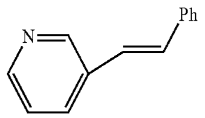
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80-7.75 (m, 3H), 7.42 (d, J=6.8 Hz, 2H), 6.34 (d, J=16.1 Hz, 1H), 3.63 (s, 3H), 2.42 (s, 3H).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.45 (m, 4H), 7.36-7.32 (m, 4H), 7.28-7.26 (m, 2H), 7.17 (d, J=12.3 Hz, 1H), 7.07 (d, J=12.3 Hz, 1H), 2.55 (s, 3H).



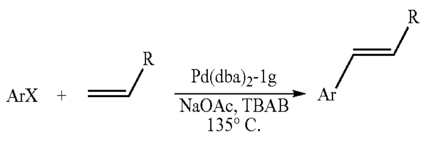
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85-7.32 (m, 15H), 6.24 (d, J=16.2 Hz, 1H).



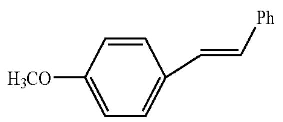
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, J=1.3 Hz, 1H), 8.45 (d, J=3.5 Hz, 1H), 7.52 (d, J=9.0 Hz, 1H), 7.36-7.33 (m, 2H), 7.30-7.25 (m, 4H), 7.10 (d, J=16.2 Hz, 1H), 7.00 (d, J=16.2 Hz, 1H).

EXAMPLE 7

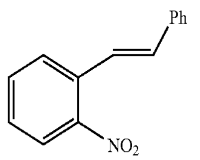
General Procedure for Heck Reaction of Deactivated Aryl Bromides and Activated Chlorides with Olefins



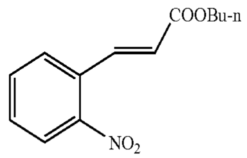
$Pd(dba)_2$ (1.5 mg, 0.0025 mmol), thiourea 1g (3.4 mg, 0.01 mmol) and sodium acetate (33 mg, 3.8 mmol) were stirred in molten TBAB (0.5 g) for 10 min at 100° C. Aryl halide (0.25 mmol, S/C=100) and olefin (0.38 mmol) were added in turn. Then the flask was sealed with a septa and heated at 135° C. After indicated time, the solution was dilute with ethyl acetate (20 mL) and washed with water and brine. Ethyl acetate was removed under vacuum and nitrobenzene (0.0128 mL) was added as internal standard. The yield of coupling product was determined by ^{1}H NMR (400 MHz or 300 MHz) analysis, by comparing the peak intensities of the α/β-H of the product and the ortho-H of nitrobenzene (internal standard).



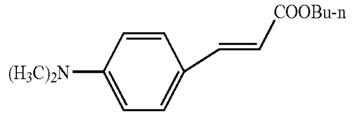
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.52 (m, 4H), 7.45-7.40 (m, 3H), 7.33 (d, J=12.1 Hz, 1H), 7.10 (d, J=12.1 Hz, 1H), 6.98 (d, J=8.2 Hz, 2H), 3.88 (s, 3H).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J=7.0 Hz, 1H), 7.74 (d, J=7.0 Hz, 1H), 7.60-7.51 (m, 5H), 7.39-7.30 (m, 3H), 7.07 (d, J=16.1 Hz, 1H).



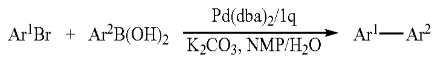
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J=17.3 Hz, 1H), 8.05 (d, J=7.8 Hz, 1H), 7.84 (d, J=6.8 Hz, 1H), 7.27-7.24 (m, 2H), 6.36 (d, J=17.3 Hz, 1H), 4.22 (t, J=5.0 Hz, 2H), 1.71-1.67 (m, 2H), 1.32-1.28 (m, 2H), 0.96 (t, J=6.8 Hz, 3H).



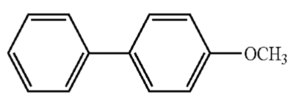
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J=15.6 Hz, 1H), 7.41 (d, J=7.1 Hz, 2H), 6.66 (d, J=7.1 Hz, 2H), 6.22 (d, J=15.6 Hz, 1H), 4.18 (t, J=6.7 Hz, 2H), 3.00 (s, 6H), 1.71-1.66 (m, 2H), 1.47-1.40 (m, 2H), 0.96 (t, J=8.2 Hz, 3H).

EXAMPLE 8

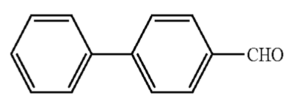
General Procedure for the Suzuki Reaction of Aryl Halides with Boric Acids



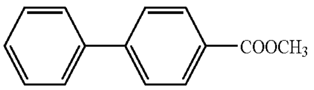
Aryliodide or bromide (0.5 mmol), arylboric acid (0.6 mmol), K_2CO_3 (1.0 mmol), bis-thiourea-$Pd(dba)_2$ 1q complex in NMP (2.5×10^{-3} M solution) and NMP/H_2O (0.75 ml/0.25 ml) were added to a flask under aerobic conditions. The flask was sealed with rubber septa and heated at the desired temperature. The reaction mixture was diluted with ethyl acetate, washed with brine, and dried over Na_2SO_4. The solvent was removed and the residue was purified by a flash chromatography on silica gel to give the product.



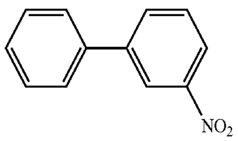
^{1}H NMR (200 MHz, $CDCl_3$) δ 7.56-7.50 (m, 4H), 7.44-7.37 (m, 2H), 7.32-7.25 (m, 1H), 6.97 (d, J=8.7 Hz, 2H), 3.84 (s, 3H).



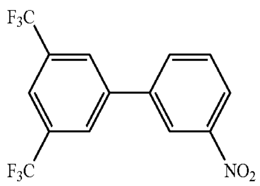
^{1}H NMR (200 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.97-7.93 (m, 2H), 7.77-7.72 (m, 2H), 7.66-7.61 (m, 2H), 7.52-7.39 (m, 3H).



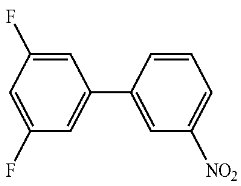
^{1}HNMR (200 MHz, $CDCl_3$) δ 8.10 (d, J=8.2 Hz, 2H), 7.68-7.60 (m, 4H), 7.49-7.36 (m, 3H), 3.93 (s, 3H).



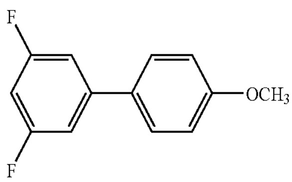
^{1}H NMR (200 MHz, $CDCl_3$) δ 8.45 (m, 1H), 8.21-8.17 (m, 1H), 7.93-7.89 (m, 1H), 7.64-7.56 (m, 3H), 7.50-7.42 (m, 3H).



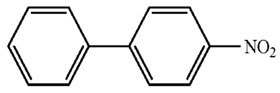
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50-8.49 (m, 1H), 8.34 (d, J=8.0 Hz, 1H), 8.06 (s, 2H), 7.98-7.95 (m, 2H), 7.73 (t, J=8.0 Hz, 1H).



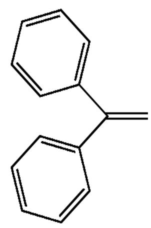
^{1}H NMR (200 MHz, $CDCl_3$) δ 8.41-8.40 (m, 1H), 8.28-8.23 (m, 1H), 7.89-7.84 (m, 1H), 7.68-7.60 (m, 1H), 7.16-7.12 (m, 2H), 6.92-6.83 (m, 1H).



^{1}HNMR (400 MHz, $CDCl_3$) δ 7.49 (d, J=8.8 Hz, 2H), 7.09-7.03 (m, 2H), 6.98 (d, J=8.8 Hz, 2H), 6.76-6.70 (m, 1H), 3.86 (s, 3H).



^{1}H NMR (200 MHz, $CDCl_3$) δ 8.29 (d, J=9.0 Hz, 2H), 7.73 (d, J=9.0 Hz, 2H), 7.60 (m, 2H), 7.52-7.40 (m, 3H).



^{1}HNMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 10H), 5.47 (s, 2H).

Notes

The following notes correspond to the superscripts contained in the application. Each of the references listed below are incorporated by reference herein.

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(5) For the use of tetraphenylphosphonium salts in Heck reactions, see: Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed.,* 1998, 37, 481.

(6) For phosphorus-free palladacycles as catalysts, see Ref. 4.

(7) For recent reviews on N-heterocyclic carbene-palladium catalysts, see: (a) Herrmann, W. A. *Angew. Chem., Int Ed.* 2002, 41, 1290. (b) Yong, B. S.; Nolan, S. P. *Chemtracts-Organic Chemistry* 2003, 205.

(8) For recent reports on Heck reactions using catalysts that are air and moisture stable, see: (a) Buchmeiser, M. R.; Wurst, K. *J. Am. Chem. Soc.* 1999, 121, 11101. (b) Silberg, J.; Schareina, T.; Kempe, R.; Wurst, K.; Buchmeiser, M. R. *J. Organomet. Chem.* 2001, 622, 6. (c) Masliorens, J.; Moreno-Manas, M.; Pla-Quintana, A.; Roglans, A. *Org. Lett.* 2003, 5, 1559.

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(14) For recent reviews on the use of ionic liquids as solvents, see: (a) Olivier-Bourbigou, H.; Magna, L. *J. Mol. Catal. A: Chem.* 2002, 182-183, 419. (b) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* 2002, 102, 3667. (c) Davis, J. H. Jr.; Fox, P. A. *Chem. Commun.* 2003, 1209.

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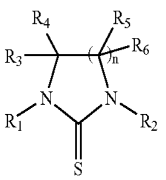
(16) (a) Darses, S.; Michaud, G.; Genet, J.-P. *Eur. J. Org. Chem.* 1999, 1875; (b) Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* 2002, 67, 8416. (b) Darses, S. Genet, J.-P. *Eur. J. Org. Chem.* 2003, 4313.

We claim:

1. An N,N'-disubstituted thiourea ligand represented by structure I:

I



wherein

n is an integer in the range of 1 to 8 inclusive;

R_1 and R_2 are independently for each occurrence cycloalkyl, aryl, aralkyl, or —$(CH_2)_m$—R_{80};

R_3, R_4, R_5, and R_6 are independently for each occurrence H, alkyl, halogenated alkyl, cycloalkyl, aryl, aralkyl, —$(CH_2)_m$—R_{80}, $COOR_v$ (where R_v=alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80}), and $CONR_uR_v$ (where R_u or R_v=H, alkyl, cycloalkyl, aryl, aralkyl, and —$(CH_2)_m$—R_{80});

R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or another polycycle;

m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and

the N,N'-disubstituted thiourea ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

2. The N,N'-disubstituted thiourea ligand of claim 1, wherein:

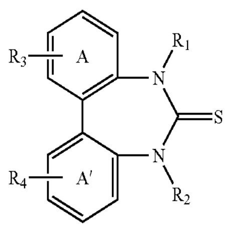
R_1 and R_2 are independently for each occurrence 2,4,6-mesityl, 2,5-di-t-butylphenyl, 2,6-diethylphenyl or t-butyl;

R_3, R_4, R_5, and R_6 are absent;

and n=1 and 2.

3. An N,N'-disubstituted thiourea ligand represented by structure II:

II



wherein

R_1 and R_2 are independently for each occurrence alkyl, cycloalkyl, aryl, aralkyl, or —$(CH_2)_m$—R_{80};

the A and A' rings of the biphenyl core independently are unsubstituted or substituted with R_3 and R_4, respectively, one, two, three, or four times;

R_3 and R_4 are independently for each occurrence H, alkyl, cycloalkyl, aryl, aralkyl, halogen, alkoxyl, —SiR_3, or —$(CH_2)_m$—R_{80};

R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or another polycycle;

m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and

the N,N'-disubstituted thiourea ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

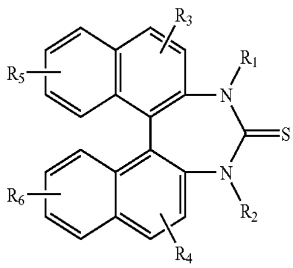
4. The N,N'-disubstituted thiourea ligand of claim 3, wherein:

R_3 and R_4 are absent, and R_1 and R_2 are independently for each occurrence benzyl, 2,4,6-trimethylbenzyl, cyclohexyl or isopropyl.

5. The N,N'-disubstituted thiourea ligand of claim 3, wherein:

R_3 and R_4 are methyl or methoxy, and R_1 and R_2 are independently for each occurrence benzyl, 2,4,6-trimethylbenzyl, cyclohexyl or isopropyl.

6. An N,N'-disubstituted thiourea ligand represented by structure III:



III

wherein

R_1 and R_2 are independently for each occurrence alkyl, cycloalkyl, aryl, aralkyl, or —$(CH_2)_m$—R_{80};

the four aryl rings of the binaphthyl core independently are unsubstituted or substituted with R_3, R_4, R_5, and R_6, respectively, any number of times up to the limitations imposed by stability and rules of valence;

R_3, R_4, R_5, and R_6 are independently for each occurrence H, alkyl, cycloalkyl, aryl, aralkyl, halogen, alkoxyl, —SiR_3, or —$(CH_2)_m$—R_{80};

R_{80} represents unsubstituted or substituted aryl, cycloalkyl, cycloalkenyl, or another polycycle;

m is independently for each occurrence an integer in the range of 0 to 8 inclusive; and

the N,N'-disubstituted thiourea ligand, when chiral, is a mixture of enantiomers or a single enantiomer.

7. The N,N'-disubstituted thiourea ligand of claim **6**, wherein:

R_3, R_4, R_5, and R_6 are absent;

R_1 and R_2 are preferentially selected, independently for each occurrence, from benzyl, 2,4,6-trimethylbenzyl, cyclohexyl and isopropyl.

8. The N,N disubstituted thiorarea ligand of claim **1**, wherein N is an integer between 1 and 8 inclusive; and R_1 and R_2 are independently for each occurrence aryl.

* * * * *