Polymeric Phosphine Ligand from Ring-Opening Metathesis Polymerization of a Norbornene Derivative. Applications in the Heck, Sonogashira, and Negishi Reactions

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Abstract: The phosphine-containing polymer **1** is obtained by ruthenium-catalyzed ring-opening metathesis polymerization of the norbornene derivative **2**. Polymer **1** is employed as the polymer support in the palladium-catalyzed Heck, Sonogashira, and Negishi reactions, and the corresponding (methoxymethylphenyl)diphenylphosphine (**6**) ligand is used for comparison. The polymer-supported catalysts retain most of their catalytic activities in these coupling reactions in the recycling processes.

The use of transition-metal catalysts immobilized on polymer supports is well-documented.[1] Catalysts can in general be recovered by filtration[2] or by biphasic separation.[3] Cross-linked styrene-based polymer supports are one of the most popular resins for this purpose. Soluble polymer supports such as those derived from polyethers,[4] polyacrylates,[5] polyethylene,[6] or fluorinated polymers[7] provide important alternative sources. To the best of our knowledge, phosphine-containing polymer supports arisen from ring-opening metathesis polymerization (ROMP) of norbornene derivatives have been sporadically explored.[8] It is noteworthy that using such phosphine-containing

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SCHEME 1 [a]
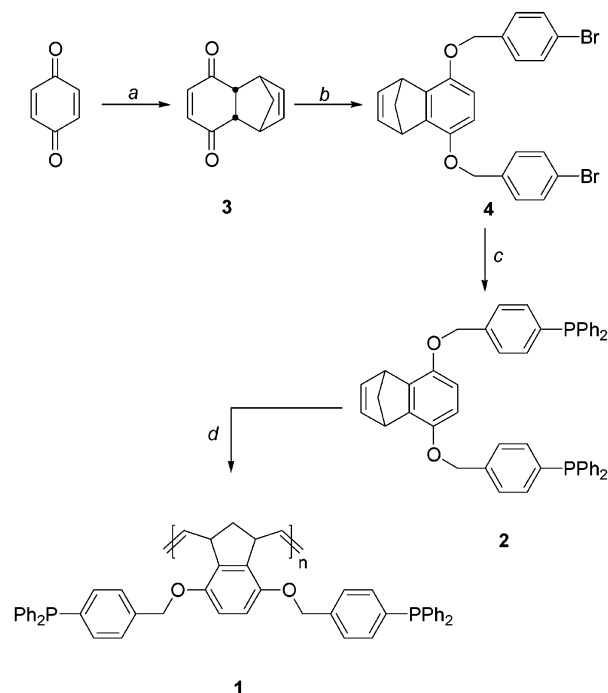
[a] (a) Cyclopentadiene, −78 °C, 95%. (b) 4-Bromobenzyl bromide, K$_2$CO$_3$, refluxing MeCN, 78%. (c) [n]BuLi, −78 °C, and then ClPPh$_2$, 60%. (d) **5**, rt.

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norbornene derivatives would make it more difficult to proceed with the ROMP reaction because the ligand on the catalyst may readily undergo exchange with the phosphine moiety on the substrates, which may reduce the activity of the catalyst.[9] It is envisaged that the recent highly reactive N-heterocyclic ruthenium carbene catalyst[10] may tolerate the presence of the phosphine moiety in the substrates.[11] We now report the synthesis of the phosphine-containing polymer **1** by ROMP of the corresponding monomer **2** and the use of **1** as the polymer-supported ligand in palladium-catalyzed C−C bond formation reactions.

Polymer **1** was prepared according to the reaction sequence shown in Scheme 1. Treatment of **3** with K$_2$CO$_3$ and 4-bromobenzyl bromide in refluxing CH$_3$CN afforded dibromide **4** in 78% yield. Reaction of **4** with [n]BuLi at −78 °C followed by displacement with ClPPh$_2$ gave the monomer **2** in 60% yield. Polymerization of **2** using second-generation Grubbs' catalyst **5**[12] in THF at room temperature for 24 h yielded the corresponding polymer **1**. Matrix-assisted laser desorption ionization time of flight (MALDI-TOF) analysis indicated that the polymer may mainly consist of 4−6 repetitive monomeric

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(12) Mes: 2,4,6-mesitylenyl. dba: dibenzylideneacetone.

**TABLE 1. Use of Phosphine Ligands 1 or 6 in the Palladium-Catalyzed Heck, Sonogashira, and Negishi Reactions**

	Heck reaction			Sonogashira reaction			Negishi reaction		
cycle	nil (%)[a]	6 (%)	1 (%)	nil (%)	6 (%)	1 (%)	nil (%)	6 (%)	1 (%)
1	63	93	95	42	93	95	42	83	85
2	15	30	90	0	34	90	0	0	76
3	0	0	87		0	86			47
4			82			79			12
5			85			65			0

[a] No phosphine ligand was added.

units.[13] ^{31}P NMR of **1** and **2** appeared as singlets at δ −5.57 and −5.24, respectively. Because each of the monomeric units contained two phosphine groups, the loading of the phosphine moiety in **1** was therefore fairly high (2.8 mmol/g). Polymer **1** is soluble in moderate polar organic solvents such as THF, toluene, or dichloromethane but insoluble in alkane solvents, ether, and DMF at room temperature. At elevated temperature, a homogeneous solution of **1** in DMF was obtained.[14]

5   **6**
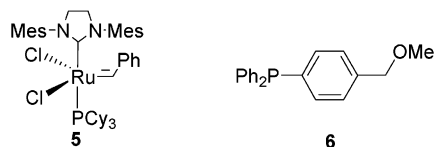
To test the efficacy of **1** as a polymer support in catalysis, a series of coupling reactions was examined. 4-(Methoxymethylphenyl)diphenylphosphine (**6**) was also used as a ligand for comparison. In the Heck reaction, a mixture of iodobenzene, methyl acrylate, and Bu$_4$NOAc in the presence of Pd(OAc)$_2$ and the phosphine ligand (**1** or **6**) in DMF was heated at 80 °C for 12 h (eq 1). After cooling to room temperature, the mixture was filtered, and the solid material was washed with ether, evacuated, and used directly for the next catalytic reaction. The filtrate was worked up as usual to afford the coupling product **7**. DMF was chosen as the solvent not only because it is a common solvent for the Heck reaction but also because the polymer ligand **1** exhibited different solubilities at different temperatures. The results are summarized in Table 1.
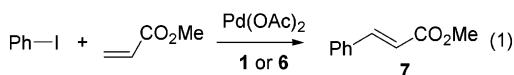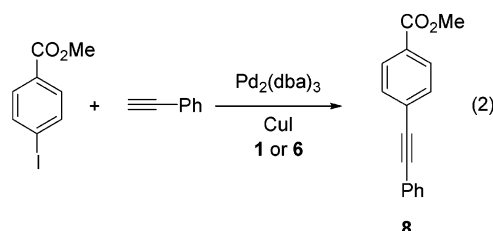

Apparently, the presence of phosphine ligands is essential to give a better yield of **7** than those without phosphines. When **6** was used, the yield of the reaction dropped from 93% in the first cycle to 30% in the second cycle, and no reaction was observed in the third cycle. Presumably, the majority of the palladium catalyst may remain in the DMF solution, and the insoluble portion was barely enough to initiate the second cycle of the Heck reaction. On the other hand, when polymer **1** was

employed, five catalytic cycles had been performed. The catalyst retained more than 90% of the activity of the catalyst in the previous cycle.

In the Sonogashira reaction, phenylacetylene was treated with methyl 4-iodobenzoate in the presence of Pd$_2$(dba)$_3$,[12] CuI, and phosphine ligand (**1** or **6**) in refluxing Et$_3$N for 12 h (eq 2). In a manner similar to that described for the Heck reaction, the mixture was worked up to give **8**, and the catalyst was recovered for the next cycle. It is noteworthy that Et$_3$NHI was also precipitated and was mixed with the catalyst for the next cycle. However, the presence of this side product did not show any appreciable effect on the reaction. The results are also outlined in Table 1. Again, the phosphine ligand is indispensable in this reaction. The monomeric ligand **6** gave an excellent yield in cycle 1, but the activity significantly decreased in the second cycle and no reaction was observed in the third cycle. The catalytic activity also gradually fell by approximately 4−8% in each recycle experiment when **1** was used.

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Negishi coupling reaction was also employed to test the activity of the polymer support **1**. 4-Cyanophenylzinc bromide was allowed to react with methyl 4-iodobenzoate in the presence of Pd(dba)$_2$[12] and phosphine ligand (**1** or **6**) in THF at room temperature for 12 h (eq 3). The mixture was poured into ether, and the precipitate was collected and washed with ether. Usual workup of the filtrate yielded the coupling product **9**. As can be seen from Table 1, no reaction occurred when the recycled catalyst with monomeric phosphine ligand was used, and the catalytic activity reduced significantly when the recycled polymer-supported catalyst (from **1**) was employed. As mentioned earlier, polymer **1** is readily soluble in THF, which may cause more difficulty in the catalyst recovery.

In summary, we have demonstrated that the phosphine-containing polymer derived from the ROMP of the norbornene derivative can serve as a polymer support for the palladium-catalyzed C−C bond formation. Further extension in other applications is in progress in our laboratory.

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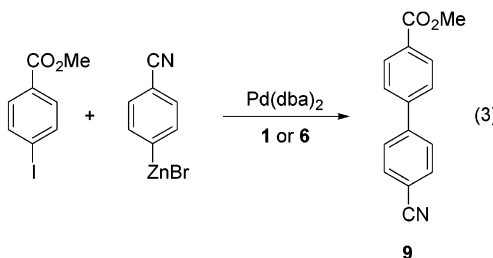
Experimental Section

1,4,4a,8a-Tetrahydro-1,4-methanonaphthalene-5,8-dione (3). To a methanol solution (40 mL) of 1,4-benzoquinone

(13) GPC analysis using polystyrene as a ref, however, gave a much lower average molecular weight (M_n = 1000, PDI = 1.1).

(14) The solubilities of **1** in DMF were 46 mg/mL at 80 °C and <0.7 mg/mL at 25 °C. The solubilities of **1** in Et$_3$N were ca. 0.2 and 0.5 mg/mL at 25 and 80 °C, respectively.

(21.62 g, 200 mmol) was added a methanol (10 mL) solution of freshly cracked cyclopentadiene (13.5 mL, 200 mmol) at −78 °C. The reaction mixture was gradually warmed to room temperature and stirred for 6 h. Removal of the solvent afforded yellow needles **3** (33.15 g, 95%). Mp: 74−76 °C (ether, lit.[15] 76−78 °C).

5,8-Bis(4-bromobenzyloxy)-1,4-dihydro-1,4-methanonaphthalene (4). A mixture of **3** (1.74 g, 10 mmol), K_2CO_3 (8.3 g, 60 mmol), and 4-bromobenzylbromide (5.0 g, 20 mmol) in CH_3-CN (100 mL) was refluxed for 36 h under a nitrogen atmosphere. The mixture was quenched with saturated NH_4Cl (150 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 × 400 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was chromatographed (CH_2Cl_2/hexane, 1:4) to give **4** as white needles (4.00 g, 78%). Mp: 182−183 °C (EtOH). ^1H NMR (400 MHz, $CDCl_3$) δ: 2.16 (d, $J = 7.0$ Hz, 1 H), 2.21 (dt, $J = 7.0$, 1.6 Hz, 1 H), 4.15 (dt, $J = 3.6$, 1.6 Hz, 2 H), 4.96 (s, 4 H), 6.48 (s, 2 H), 6.77−6.79 (m, 2 H), 7.28 and 7.50 (AA′XX′, $J = 8.1$, 0.3, 2.1, 2.1 Hz, 8 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 47.1, 69.9, 70.7, 111.8, 121.6, 129.0, 131.5, 136.6, 141.5, 142.8, 147.9. IR (KBr) ν: 3059, 3001, 2969, 2935, 2885, 2853, 1489, 1454, 1408, 1372, 1300, 1260, 1225, 1202, 1166, 1117, 1091, 1067, 1011, 978, 907, 895, 834, 808, 787, 731, 494, 481 cm^{-1}. MS (FAB) m/z (relative intensity): 514 (12), 512 (23), 510 (M$^+$, 11), 171 (40), 169 (41), 155 (47), 139 (22), 138 (33), 137 (100), 124 (11), 120 (19), 97 (12), 95 (13), 91 (25), 83 (14), 77 (22), 57 (16). HRMS calcd for $C_{25}H_{20}Br_2O_2$: 509.9830. Found: 509.9824. Anal. Calcd: C, 58.62; H, 3.94. Found: C, 58.43; H, 3.77.

5,8-Bis(4-diphenylphosphoranylbenzyloxy)-1,4-dihydro-1,4-methanonaphthalene (2). Under an argon atmosphere, a THF solution (20 mL) of **4** (1.53 g, 3 mmol) was treated with ^nBuLi (3.0 mL of a 2.5 M solution, 7.5 mmol) and stirred at −78 °C for 30 min. A THF solution (20 mL) of chlorodiphenylphosphine (1.50 mL, 8 mmol) was then added to the reaction mixture at −78 °C. After 1 h, the mixture was gradually warmed to room temperature and stirred for 5 h. The reaction was quenched with saturated NH_4Cl (30 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with water (50 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo to afford the crude product, which was chromatographed on silica gel (CH_2Cl_2/hexane, 1:2) to furnish **2** as white needles (0.43 g, 60%). Mp: 146−147 °C (EtOH). ^1H NMR (400 MHz, $CDCl_3$) δ: 2.12 (dt, $J = 7.0$, 1.4 Hz, 1 H), 2.17 (dt, $J = 7.0$, 1.6 Hz, 1 H), 4.14 (dt, $J = 3.7$, 1.5 Hz, 2 H), 4.99 (s, 4 H), 6.51 (s, 2 H), 6.74 (t, $J = 1.8$ Hz, 2 H), 7.27−7.37 (m, 28 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 47.1, 70.0, 71.3, 112.0, 127.4 (d, $J = 7.2$ Hz), 128.5 (d, $J = 6.8$ Hz), 128.7, 133.7 (d, $J = 19.2$ Hz), 133.9 (d, $J = 19.4$ Hz), 136.7 (d, $J = 11.1$ Hz), 137.1 (d, $J = 10.7$ Hz), 138.3, 141.5, 142.9, 148.1. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −5.24. IR (KBr) ν: 3068, 3000, 2933, 2866, 1585, 1490, 1459, 1433, 1400, 1301, 1256, 1164, 1116, 1090, 1043, 1017, 908, 810, 743, 696, 505 cm^{-1}. MS (FAB) m/z (relative intensity): 723 (M + H$^+$, 53), 722 (M$^+$, 40), 292 (13), 289 (13), 277 (10), 276 (53), 275 (100), 197 (16), 185 (13), 183 (20), 167 (22), 165 (17), 155 (18), 138 (18), 137 (34), 121 (17), 107 (10). HRMS calcd for $C_{49}H_{41}O_2P_2$ (M + H$^+$): 723.2599. Found: 723.2582. Anal. Calcd for $C_{49}H_{40}O_2P_2$: C, 81.42; H, 5.58. Found: C, 81.17; H, 5.45.

Synthesis of Polymer 1. In a glovebox, to a THF solution (5 mL) of **3** (361 mg, 0.5 mmol) was added **5** (21 mg, 0.025 mmol), and the mixture was stirred at room temperature for 24 h and then poured into pentane (50 mL) to form a pink suspension. The suspension was centrifuged, and the pink precipitate was collected. The precipitate was dissolved in 2 mL of CH_2Cl_2 and reprecipitated in pentane (20 mL) before centrifuging. The reprecipitation was repeated a few times to provide **1** as a pale yellowish white powder (325 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ: 1.25−1.85 (br, 1H), 2.15−2.75 (br, 1H), 3.45−4.45 (br, 2H), 4.45−5.15 (br, 4H), 5.28−5.90 (br, 2H), 6.00−6.50 (br, 2H), 6.60−7.80 (br, 28H). ^{31}P NMR (121 MHz, $CDCl_3$) δ: −5.57. IR (KBr) ν: 2959, 2919, 1488, 1456, 1434, 1398, 1379, 1260, 1184,

1017, 806, 743, 694, 539 cm^{-1}. MALDI-TOF MS (dithranol) m/z (relative intensity): 2356 (53), 3110 (100), 3865 (77), 4619 (23), 5373 (6), 6128 (3).

(4-Methoxymethylphenyl)diphenylphosphane (6). Under an argon atmosphere, a THF solution (20 mL) of 1-bromo-4-methoxymethylbenzene (4.02 g, 20 mmol) was treated with ^nBuLi (10 mL of a 2.5 M solution, 25 mmol) at −78 °C, and the mixture was stirred for 30 min. A THF solution (10 mL) of chlorodiphenylphosphine (5.40 mL, 30 mmol) was then introduced at −78 °C. After 1 h, the mixture was gradually warmed to room temperature, stirred for 5 h, and quenched with saturated NH_4Cl (30 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with water (50 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo to afford the crude product, which was chromatographed on silica gel (hexane/CH_2Cl_2, 1:4) to give **6** as a colorless oil (5.58 g, 91%). ^1H NMR (400 MHz, $CDCl_3$) δ: 3.40 (s, 3 H), 4.45 (s, 2 H), 7.26−7.35 (m, 14 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 58.2, 74.3, 127.7 (d, $J = 7.1$ Hz), 128.4 (d, $J = 6.9$ Hz), 128.6, 133.8 (d, $J = 19.1$ Hz), 133.9 (d, $J = 19.4$ Hz), 136.4 (d, $J = 10.5$ Hz), 137.1 (d, $J = 10.5$ Hz), 138.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −5.24.

Heck Reaction. A DMF suspension (10 mL) of tetrabutylammonium acetate (0.75 g, 2.5 mmol) and crushed 4A molecular sieve (0.4 g) was stirred for 15 min. Phosphine **1** (36.1 mg, 0.05 mmol), iodobenzene (0.11 mL, 1.0 mmol), and methyl acrylate (0.18 mL, 2 mmol) were then successively added to the mixture, and the mixture were stirred for another 15 min before addition of palladium acetate (11.2 mg, 0.05 mmol). The reaction mixture was stirred at 80 °C for 12 h and then filtered on filter paper. The insoluble materials were washed with Et_2O (50 mL) and collected for subsequent runs. The filtrate was extracted with water (50 mL). The aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with saturated NH_4Cl (50 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo to afford the crude product. The crude product was purified by flash column chromatography (CH_2Cl_2/hexane, 1:4) and recrystallized from ethanol to provide **7** as a white solid (0.15 g, 95%). Mp: 34−35 °C (lit.[16] 35−36 °C).

A similar procedure was employed when phosphine **6** was used.

Sonogashira Reaction. To methyl 4-iodobenzoate (262 mg, 1.0 mmol) in Et_3N (10 mL) was added $Pd_2(dba)_3\cdot CHCl_3$ (26 mg, 0.025 mmol) and phosphine **1** (36.1 mg, 0.10 mmol). The reaction mixture was bubbled with nitrogen for 10 min followed by the addition of phenylacetylene (0.11 mL, 1.1 mmol) and CuI (4.8 mg, 0.025 mmol). The mixture was refluxed for 12 h. After cooling to room temperature, the mixture was filtered on filter paper. The insoluble materials were washed with Et_2O (50 mL) and collected for subsequent runs. The filtrate was added to a saturated NH_4Cl solution (50 mL), and the organic layer was separated. The organic layer was washed with saturated NH_4-Cl (3 × 50 mL), dried ($MgSO_4$), filtered, and evaporated in vacuo to afford the crude product, which was chromatographed on silica gel (CH_2Cl_2/hexane, 1:4) to give **8** as a white solid (0.22 g, 95%). Mp: 120−121 °C (EtOH, lit.[17] 124 °C).

A similar procedure was employed when phosphine **6** was used.

Negishi Reaction. 4-Bromobenzonitrile (457.4 mg, 1.2 mmol) in THF (10 mL) was treated with ^nBuLi (0.5 mL of a 2.5 M solution, 1.25 mmol) at −78 °C for 30 min. $ZnBr_2$ (292 mg, 1.3 mmol) in THF (5 mL) was then added at −78 °C, and after being stirred for 5 min, the mixture was slowly warmed to 0 °C and then transferred via a cannula to another flask containing Pd-(dba)$_2$ (23 mg, 0.04 mmol), phosphine **1** (57.8 mg, 0.08 mmol), and methyl 4-iodobenzoate (262 mg, 1.0 mmol) in THF (10 mL). The mixture was then warmed to room temperature and stirred for 12 h. Et_2O (50 mL) was added, and the mixture was filtered on filter paper. The insoluble materials were washed with Et_2O (50 mL) and collected for subsequent runs. The filtrate was extracted with saturated NH_4Cl (3 × 100 mL), dried ($MgSO_4$),

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filtered, and evaporated in vacuo to afford the crude product, which was chromatographed on silica gel (CH$_2$Cl$_2$/hexane, 1:1) to give **9** as a white solid (0.20 g, 85%). Mp: 104−105 °C (EtOH, lit.[18] 102−103 °C).

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A similar procedure was employed when phosphine **6** was used.

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