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Tetrahedron 59 (2003) 3467–3473

TETRAHEDRON

A palladium complex with a new hemilabile amino- and sulfur-containing phosphinite ligand as an efficient catalyst for the Heck reaction of aryl bromides with styrene. The effect of the amino group

Ioannis D. Kostas,[a,*] Barry R. Steele,[a,*] Aris Terzis[b] and Svetlana V. Amosova[c]

[a]*National Hellenic Research Foundation, Institute of Organic and Pharmaceutical Chemistry, Vas. Constantimou 48, 116 35 Athens, Greece*
[b]*Institute of Materials Science, NCSR Democritos, 153 10 Aghia Paraskevi Attikis, Greece*
[c]*Favorsky Irkutsk Institute of Chemistry, Siberian Branch of Russian Academy of Sciences, 1 Favorsky Street, 664033 Irkutsk, Russian Federation*

Received 23 January 2003; revised 27 February 2003; accepted 21 March 2003

Dedicated to Professor Dr Manfred T. Reetz on the occasion of his 60th birthday and in recognition of his important contributions to chemistry

Abstract—A palladium complex with a new hemilabile amino- and sulfur-containing phosphinite ligand has been synthesised and its crystal structure determined. This system efficiently catalyses the Heck reaction of aryl bromides with styrene at 130°C after 24 h, with turnover numbers of up to 100000 and with a selectivity towards *trans*-stilbenes ranging from 91.5 to 96.3%. The analogous sulfur-containing phosphinite without the amino group has also been synthesised and subjected to the Heck reaction. The constructive role of the amino group on the formation of the *P*,*S*-chelate palladium complex as well as in the Heck reaction is discussed. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

The palladium-catalysed arylation of alkenes, nowadays known as the Heck reaction, is one of the most versatile tools of organic chemistry for C–C bond forming reactions.[1] The reactivity decreases drastically in the order ArI>ArBr>ArCl and, for that reason, aryl bromides and chlorides, while being cheaper and more readily available and therefore much more useful substrates to synthetic chemists, often do not react efficiently. In recent years, however, aryl bromides and chlorides have been successfully applied using a variety of catalytic systems involving, for example, several types of phosphorus-free ligands,[2] monodentate phosphorus ligands,[3] phosphorus or phosphorus–heteroatom bi- or polydentate ligands,[4] or traditional Heck coupling catalysts combined with additives[5] or with new techniques.[6]

The improved catalytic activity of transition metal complexes with hemilabile ligands has been extensively reviewed.[7] Up to now, however, the use of such ligands in the Heck reaction has been limited.[4j,8] We have recently reported the synthesis of several functionalised hemilabile *P*,*N*-, *P*,*N*,*P*- and *N*,*P*,*N*-ligands (**1**–**6**) and their application in rhodium-catalysed hydroformylation, hydroaminomethylation and hydrogenation (Fig. 1).[9–12]

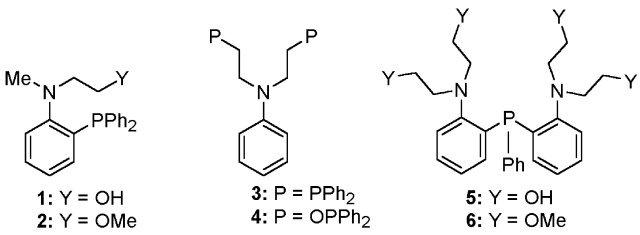

Figure 1.

As an extension of this research, we report here the synthesis and crystal structure of a palladium complex with a new hemilabile amino- and sulfur-containing phosphinite ligand. This system was found to efficiently catalyse the Heck reaction of aryl bromides with styrene. In order to investigate the influence of the amino group on the catalyst behaviour, we have also synthesised the analogous sulfur-containing phosphinite without the amino group. The effect of the amino group on the formation of the palladium complex as well as in the Heck reaction is discussed. Although phosphinites as ligands in homogeneously

Keywords: Heck reaction; hemilabile ligand; *P*,*S*-ligand; phosphinite; palladium complex; crystal structure.
* Corresponding authors. Tel.: +30-210-7273878; fax: +30-210-7273877; e-mail: ikostas@eie.gr (I.D.K.); bsteele@eie.gr (B.R.S.)

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doi:10.1016/S0040-4020(03)00474-5

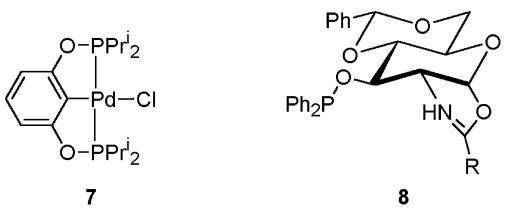


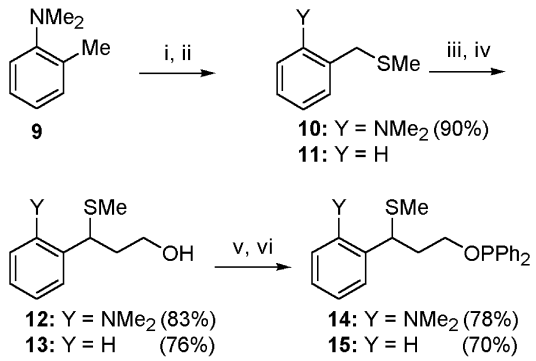
Figure 2.

catalytic processes have been widely studied,[11,13] their application in the Heck reaction is limited to a palladium bis(phosphinite) PCP–pincer complex **7**[4c] and to palladium complex catalysis involving phosphinite-oxazoline ligands **8** derived from D-glucosamine[14] (Fig. 2).

2. Results and discussion

2.1. Synthesis of the ligands

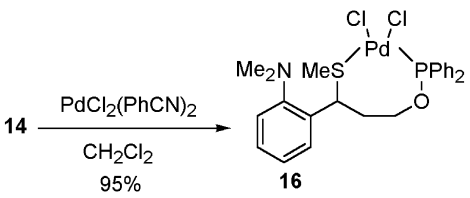
The synthesis of ligands **14** and **15** is outlined in Scheme 1. The ligand precursor **14** was prepared in a multistep procedure from *N*,*N*-dimethyl-*o*-toluidine (**9**), in an overall yield of 58%. *ortho*-Metallation of **9** by *n*-BuLi and subsequent quench with dimethyl disulfide yielded the thioether **10**, which was then subjected to metallation at the benzylic carbon with *n*-BuLi/TMEDA and subsequent reaction with ethylene oxide to give the functionalised alcohol **12**. The phosphinite ligand **14** was prepared by hydrogen abstraction of **12** using *n*-BuLi and subsequent reaction of the resulting alkoxide with $ClPPh_2$. Phosphinite **15** was prepared by the same procedure from benzyl methyl sulfide (**11**) in an overall yield of 53%.



Scheme 1. *Reagents and conditions*: (i) *n*-BuLi, Et_2O, room temperature to 35°C; (ii) Me_2S_2, 0°C to room temperature; (iii) *n*-BuLi/TMEDA, methylcyclohexane, −10°C; (iv) ethylene oxide, Et_2O, −10°C to room temperature; (v) *n*-BuLi, THF, −78°C to room temperature; (vi) Ph_2PCl, THF, 0°C to room temperature.

2.2. Synthesis and characterization of the palladium complexes

Treatment of $PdCl_2(NCPh)_2$ in a dichloromethane solution with 1 equiv. of ligand **14** yielded the palladium complex **16** in high yield (Scheme 2). The solution ^1H and ^{13}C NMR spectra indicated that the ligand is *P*,*S*-bonded and that the nitrogen is situated away from the coordination sphere around palladium. The SCH_3 resonances are shifted to low field compared to those in the free ligand, in contrast to the



Scheme 2.

$N(CH_3)_2$ resonances which are in almost the same position in both the complex and the free ligand, indicating the absence of Pd–N interaction.

Yellow crystals of complex **16** suitable for X-ray crystal structure determination were obtained by slow diffusion of ether through a diluted solution of **16** in dichloromethane. Its structure is shown in Figure 3. As shown in the crystal structure, the ligand is coordinated to the metal in a *P*,*S*-bidentate mode without any Pd–N interaction. The coordination sphere around palladium can be regarded as slightly distorted square planar (P–Pd–S, 95.41(2)°; S–Pd–Cl(1), 81.16(3)°; Cl(1)–Pd–Cl(2), 91.51(3)°; Cl(2)–Pd–P, 91.89(3)°). The Pd–P and Pd–S distances of 2.231(1) and 2.297(1) Å, respectively, have normal values, and the difference in bond lengths between the Pd–Cl(1) *trans* to P (2.369(1) Å) and Pd–Cl(2) *trans* to S (2.292(1) Å) is the result of the greater structural *trans* influence of phosphorus compared to sulfur donor.[4j]

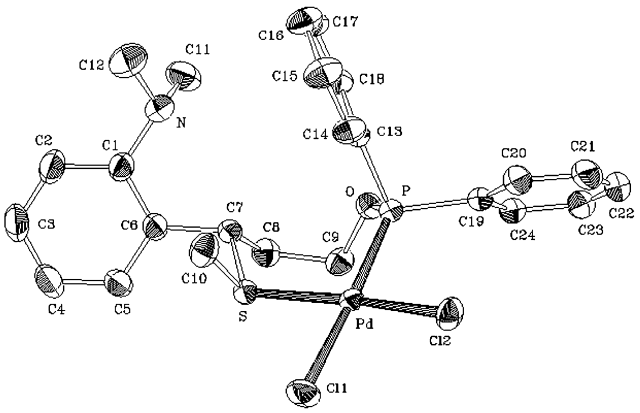
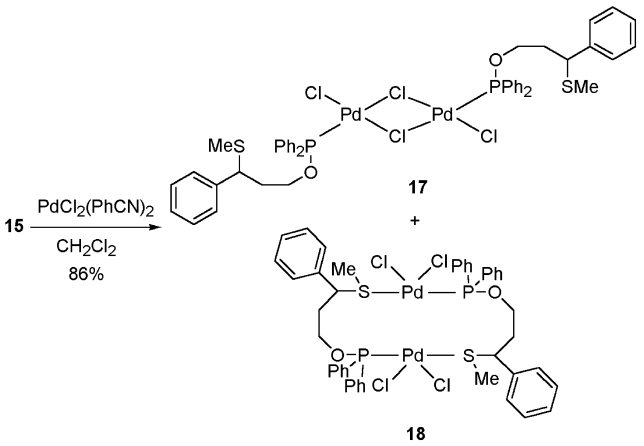


Figure 3. ORTEP drawing of palladium complex **16**.

Unfortunately, all attempts to synthesise an analogous chelate palladium complex with ligand **15** were unsuccessful. Treatment of $PdCl_2(NCPh)_2$ with 1 equiv. of ligand **15**, as described above for the synthesis of **16**, led to a yellow solid, the NMR data of which need some comments. The SCH_3 group gave two singlet peaks at δ 2.29 and 1.97 in the ^1H NMR spectrum, and also two singlet peaks at δ 21.93 and 15.24 in the ^{13}C NMR spectrum. The SCH_3 resonances at low field indicate the existence of a coordinated group while the higher field resonances which have shifts comparable to those of the free ligand, indicate the presence of non-coordinated groups. In addition, the ^{13}C NMR spectrum displays two peaks for each of the non-aromatic carbons and the ^{31}P NMR spectrum exhibits two singlets at δ 111.12 and 113.03, which are at higher field compared to the chemical shift of 119.75 for the *P*,*S*-chelate palladium complex **16**, indicating that an analogous chelation for the ligand **15** is



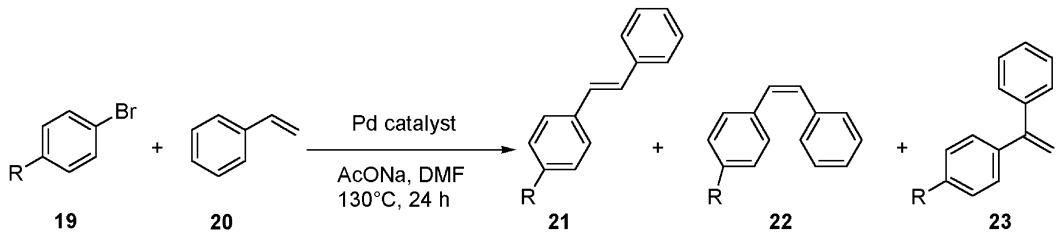
Scheme 3.

not present. These data indicate that treatment of $PdCl_2(NCPh)_2$ with **15** gives a mixture of two complexes for which a seven-membered *P*,*S*-chelate ring must be excluded. Since sulfur is coordinated to the metal in one of these complexes and not in the other, the above-mentioned observations, in combination with the elemental analysis data, are consistent with the formation of the dimeric structures **17** and **18** shown in Scheme 3. For reasons which have not yet been understood, it is apparent that the dimethylamino group on ligand **14** directs the formation of the *P*,*S*-chelate complex and that this is not possible for this system where the group is absent. This may perhaps be due to steric effects.

2.3. Heck reaction

Complex **16** was applied to the Heck reaction of styrene with several 4-substituted aryl bromides (from electron-rich to electron-poor) in DMF at 130°C for 24 h, using AcONa as base, and in the absence of any promoting additive such as *n*-Bu_4NBr (Scheme 4, Table 1). Since **16** is sensitive towards air and moisture, the efficient exclusion of air and the use of pure and dry solvent and Heck reactants was necessary. Phosphinites are also known to be sensitive towards alcohols and thus the application of **16** to the Heck reaction of 4-bromophenol failed. Catalysis was performed using a stock solution of **16**, avoiding the separate in situ addition of the palladium source and the ligand to the reactants, following the procedure which has previously been recommended by Shaw and Perera for Pd-chelating diphosphine catalysts.[4a] The advantages of using chelating ligands in the Heck reaction have been reviewed elsewhere.[1a,b]

The reaction was first performed using a 1:1000 catalyst–aryl bromide molar ratio to ensure a higher yield process, and then by decreasing the ratio to 1:100000. The conversions were analysed by GC and, for some cases, the yield refers to the isolated product, indicating the synthetic value of our catalytic system. There was good selectivity towards *trans*-stilbenes **21**, ranging from 91.5 to 96.3%, and it is noteworthy that side-products such as biphenyl were absent or present only in traces. As expected, the catalytic activity depends on the halide, while electron-withdrawing groups on the aryl ring increase the reaction rate.[1] A catalyst–substrate ratio of 1:1000 leads to total yields of



Scheme 4.

Table 1. Heck reaction of aryl bromides with styrene catalysed by palladium complex **16**

Entry	R	ArBr/Pd ratio	Yield (%)[a]	TON[b]	Selectivity **21** : **22** : **23**
1	OMe	1000	13.3	133	91.5 : – : 8.5
2	OMe	100000	5.7	5700	92.8 : – : 7.2
3[c]	H	1000	39.3 (30)[d]	393	92.8 : 1.0 : 6.2
4	H	100000	11.6	11600	96.3 : 0.4 : 3.3
5	Cl	1000	90.4	904	93.4 : 0.9 : 5.7
6	Cl	100000	81.3	81300	93.5 : 0.8 : 5.7
7	CHO	1000	98.4	984	96.1 : 0.7 : 3.2
8	CHO	100000	82.6	82600	95.4 : 0.8 : 3.8
9[c]	CN	1000	100.0 (90)[d]	1000	95.6 : 0.2 : 4.2
10	CN	100000	81.9	81900	95.3 : 0.7 : 4.0
11[c]	NO_2	1000	100.0 (94)[d]	1000	95.8 : 0.3 : 3.9
12[c]	NO_2	100000	100.0 (90)[d]	100000	96.3 : 0.2 : 3.5

Reaction conditions: ArBr (1.0 mmol), styrene (1.5 mmol), AcONa (2.0 mmol), Pd complex **16** in DMF (1 mL), 130°C, 24 h.
[a] Total GC yield of all isomers, based on the aryl bromide using decane as internal standard.
[b] Turnover no. (TON)=fraction of products (**21**+**22**+**23**)×substrate/Pd ratio.
[c] The reaction was performed on a 10-fold scale.
[d] Isolated yield.

Table 2. Heck reaction of aryl bromides with styrene catalysed by in situ $PdCl_2(PhCN)_2$ and ligand **14** or **15**

Entry	Ligand	R	ArBr/Pd ratio	Yield (%)[a]	TON[b]	Selectivity **21** : **22** : **23**
1[c]	**14**	H	1000	31.9 (25)[d]	319	93.3 : 0.2 : 6.5
2[c]	**15**	H	1000	27.1 (22)[d]	271	94.0 : 0.3 : 5.7
3	**14**	CHO	100000	59.6	59600	95.9 : 0.1 : 4.0
4	**15**	CHO	100000	51.6	51600	95.4 : 0.3 : 4.3
5	**14**	NO_2	100000	66.8	66800	95.9 : 0.2 : 3.9
6	**15**	NO_2	100000	55.9	55900	96.1 : – : 3.9

Reaction conditions: ArBr (1.0 mmol), styrene (1.5 mmol), AcONa (2.0 mmol), $PdCl_2(PhCN)_2$ and ligand (1:1) mixed in situ, DMF (1 mL), 130°C, 24 h.
[a] Total GC yield of all isomers, based on the aryl bromide using decane as internal standard.
[b] Turnover no. (TON)=fraction of products (**21**+**22**+**23**)×substrate/Pd ratio.
[c] The reaction was performed on a 10-fold scale.
[d] Isolated yield.

13.3 and 39.3% for bromoanisole and bromobenzene, respectively. At lower ratios for these substrates, the reaction proceeds with TONs up to 5700 and 11600, respectively. High activity was observed for activated aryl bromides. A catalyst–substrate ratio of 1:1000 leads to high or quantitative conversion of the aryl bromide, and with a ratio of 1:100000, the reaction proceeds with TONs up to 100000. At lower ratios, even higher TONs are possible but these were not optimised. Although the Heck reaction can be performed at lower temperatures, 130°C is the best reaction temperature for synthetic purposes. For some of the activated bromides the reaction proceeds even at room temperature without any additive but with considerably lower reaction rates and, for that reason, are not of synthetic importance.

Since it was not possible to synthesise the analogous chelate palladium complex with ligand **15**, the catalytic activity of the latter towards Heck reaction was investigated for a representative range of substrates by mixing in situ $PdCl_2(NCPh)_2$ and **15** (1:1) in DMF, using the same reaction conditions and reactant concentrations, as described above for complex **16** (Table 2). For comparison purposes, the Heck reaction was also performed my mixing in situ $PdCl_2(NCPh)_2$ and ligand **14** (1:1) (Table 2). As expected, and for reasons which have been mentioned elsewhere, the catalytic activity of the in situ system $PdCl_2(NCPh)_2$/**14** is lower than complex **16**.[4a] As shown in Table 2, the *N*,*S*-phosphinite ligand **14** leads to higher TONs in comparison with those obtained with the *S*-phosphinite ligand **15**, without a significance difference in the selectivity towards *trans*-stilbenes. For the activated aryl bromides, the higher activity of **14** compared to **15** is clear for a substrate–Pd ratio of 100000:1. Although, the constructive role of the amino group in catalysis has not been clarified, it is presumably due to the stabilising chelate effect with ligand **14**, since an analogous *P*,*S*-chelation with ligand **15** was not possible. In addition, despite the absence of Pd–N coordination in complex **16** or the system formed by mixing ligand **14** and the palladium source in situ, the existence of an additional coordination site as a stabilizing group during the course of a metal-mediated reaction could improve the catalytic efficiency of the complex. The higher activity of complexes with nitrogen-containing phosphines in which nitrogen is not bound to the metal compared with the analogous ligands without nitrogen has previously been noted by Reetz et al. for rhodium-catalysed hydroformylation.[15]

3. Conclusions

In summary, a seven-membered chelate palladium complex with a new hemilabile amino- and sulfur-containing phosphinite ligand has been prepared. According to the NMR data and its crystal structure, the ligand is bound to the metal in a *P*,*S*-bidentate coordination mode without any Pd–N interaction. This complex was found to efficiently catalyse the Heck reaction of aryl bromides with styrene, with high turnover numbers and a good selectivity towards *trans*-stilbenes. Especially for the electron-poor aryl bromides, a low catalyst loading as little as 0.001 mol% was sufficient to mediate a high yield Heck reaction. The low catalyst loading represents an environmentally friendly procedure and could become important for industrial processes. Attempts to synthesise a *P*,*S*-chelate palladium complex with the analogous sulfur-containing phosphinite ligand without the amino group failed, indicating the constructive role of this group in the formation of a *P*,*S*-chelation in this system, and this may be due to steric effects. The catalytic activity of the latter ligand mixed in situ with $PdCl_2(NCPh)_2$ was found to be lower compared with the analogous amino-substituted ligand. The constructive role of the amino group in catalysis is presumably due to the stabilizing chelate effect of the complex, since a *P*,*S*-chelation could not be achieved without this group, as well as to the existence of nitrogen as an additional coordination site as a stabilizing group during the course of the metal-mediated reaction.

4. Experimental

4.1. General

Bis(benzonitrile)dichloropalladium was prepared according to a literature procedure.[16] *n*-BuLi was prepared from lithium metal and *n*-BuCl in methylcyclohexane. All the other reagents were commercially available. All preparations and catalysis were carried out under argon by using dry and degassed reagents and solvents. NMR: Bruker AC 300 (300.13, 75.47, and 121.50 MHz for ^1H, ^{13}C and ^{31}P, respectively); ^1H and ^{13}C NMR shifts were referenced to the solvents and the ^{31}P NMR shifts were referenced to external 85% H_3PO_4 in D_2O. The determination of the CH, CH_2 and CH_3 carbons in the ^{13}C NMR spectra was performed by DEPT-NMR experiments. IR: Bruker Equinox 55. ESI MS: Finnigan MAT TSQ 7000. GC-MS

(EI): Varian Saturn 2000 with a 30 m×0.25 mm DB5-MS column. GC: Varian Star 3400 CX with a 30 m×0.53 mm DB5 column. Elemental analyses for C, H, N: Perkin–Elmer PE 2400 II.

4.2. Syntheses of compounds 10, 12–18

4.2.1. 2-[(Methylthio)methyl]-*N*,*N*-dimethylbenzenamine (10). *n*-BuLi (1.91 M in methylcyclohexane, 75 mL, 143.3 mmol) was added to a solution of *N*,*N*-dimethyl-*o*-toluidine (**9**) (14.5 mL, 99.6 mmol) in ether (50 mL). The reaction mixture was refluxed for 8 h and subsequently stirred at room temperature overnight. A solution of dimethyl disulfide (13.2 mL, 148.5 mmol) in ether (30 mL) was then added dropwise within 1 h with ice-water bath cooling, and the mixture stirred at room temperature overnight. Water was then added, the product was extracted with ether, dried over Na_2SO_4, filtered and evaporated to dryness. Purification was carried out by distillation, yielding **10** (16.3 g, 90.1 mmol, 90%) as a colourless oil, bp 69–70°C (0.2 mbar). IR (neat): ν 3065, 3020, 2978, 2935, 2920, 2863, 2830, 2785, 1598, 1490, 1454, 1305, 1155, 1045, 945, 760 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.42 (d, ^3J=7.4 Hz, 1H, Ar), 7.23–7.03 (m, 3H, Ar), 3.86 (s, 2H, CH_2), 2.72 (s, 6H, $N(CH_3)_2$), 2.09 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 152.98, 133.00, 130.42, 127.59, 123.40 and 119.64 (Ar), 45.21 ($N(CH_3)_2$), 33.50 (CH_2), 15.61 (SCH_3); GC-MS (EI): *m*/*z* (relative intensity) 181 (M^+, 45), 166 (20), 134 (100), 118 (39), 91 (24), 45 (13). Anal. calcd for $C_{10}H_{15}NS$: C, 66.25; H, 8.34; N, 7.73. Found: C, 65.81; H, 8.54; N, 7.88.

4.2.2. 2-[(1-Methylthio-3-hydroxy)propyl]-*N*,*N*-dimethyl-benzenamine (12). *n*-BuLi (1.91 M in methylcyclohexane, 32 mL, 61.1 mmol) was added dropwise over 30 min to a solution of **10** (9.1 g, 50.3 mmol) and TMEDA (5 mL, 33.1 mmol) in methylcyclohexane (20 mL) with an ice-salt cooling bath (temperature <-10°C), and stirred at this temperature for an additional 1.5 h, yielding a pale yellow suspension. Ether (50 mL) was then added. Ethylene oxide (ca. 3 mL, 60 mmol) was condensed into a Schlenk tube connected to the reaction flask via tubing and then allowed to evaporate slowly (over 20 min) into the ice-salt cooled reaction mixture which became slightly yellower. After the addition was complete, the reaction mixture was allowed to warm up slowly to room temperature and stirred overnight. It was then poured into water and extracted with dichloromethane. The organic extracts were washed with water, dried over Na_2SO_4, filtered and evaporated to dryness. Purification was carried out by distillation, yielding **12** (9.4 g, 41.8 mmol, 83%) as a colourless oil, bp 114–117°C (0.2 mbar). IR (neat): ν 3405, 3065, 3026, 2940, 2867, 2830, 2790, 1598, 1490, 1454, 1300, 1160, 1050, 945, 755 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.55 (d, ^3J=7.5 Hz, 1H, Ar), 7.24–7.11 (m, 3H, Ar), 4.60–4.54 (m, 1H, CH), 3.74 (br s, 1H, OH), 3.58–3.54 (m, 1H, CH_2), 3.22–3.14 (m, 1H, CH_2), 2.70 (s, 6H, $N(CH_3)_2$), 2.32–2.24 (m, 1H, CH_2), 2.02 (s, 3H, SCH_3), 1.72–1.64 (m, 1H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 152.08, 136.41, 128.19, 127.83, 125.38 and 119.11 (Ar), 59.66 (CH_2O), 45.76 ($N(CH_3)_2$), 40.70 (CH), 40.07 (CH_2), 14.84 (SCH_3); GC-MS (EI): *m*/*z* (relative intensity) 225 (M^+, 5), 178 (100), 134 (49), 117 (20), 91 (10), 45 (10). Anal. calcd for $C_{12}H_{19}NOS$: C, 63.96; H, 8.50; N, 6.22. Found: C, 64.28; H, 8.75; N, 6.02.

4.2.3. 3-Methylthio-3-phenyl-1-propanol (13). Using a similar procedure to that described for the synthesis of **12**, compound **13** was prepared from benzyl methyl sulfide **11** (13.8 g, 100.0 mmol), in a yield of 76% (13.8 g, 75.8 mmol), as a colourless oil, bp 113–114°C (0.5 mbar). IR (neat): ν 3362, 3065, 3031, 2915, 2881, 1604, 1495, 1455, 1430, 1040, 960, 756, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30–7.23 (m, 5H, Ar), 3.87 (t, ^3J=7.3 Hz, 1H, CH), 3.71–3.68 (m, 1H, CH_2), 3.61–3.55 (m, 1H, CH_2), 2.30 (br s, 1H, OH), 2.15–2.04 (m, 2H, CH_2), 1.86 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 141.89, 128.47, 127.72 and 127.11 (Ar), 60.40 (CH_2O), 47.89 (CH), 38.41 (CH_2), 14.08 (SCH_3); GC-MS (EI): *m*/*z* (relative intensity) 181 ($[M-H]^+$, 18), 134 (86), 117 (20), 105 (100), 91 (54), 77 (27), 45 (14). Anal. calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found: C, 65.51; H, 7.88.

4.2.4. 2-[1-Methylthio-3-[(diphenylphosphino)oxy]propyl]-*N*,*N*-dimethyl-benzenamine (14). *n*-BuLi (1.80 M in methylcyclohexane, 8 mL, 14.4 mmol) was added to a solution of **12** (3.1 g, 13.8 mmol) in THF (30 mL) at −78°C. The reaction mixture was stirred at room temperature 20 min and subsequently a solution of chlorodiphenylphosphine (2.6 mL, 14.5 mmol) in THF (10 mL) was added dropwise with ice-water cooling, and the mixture then stirred at room temperature overnight. The volatile materials were removed by evaporation, the residue was suspended in toluene (100 mL) and filtered to remove the inorganic salts. The solution was then passed through a short column of neutral alumina. Evaporation of the solvent under reduced pressure afforded **14** as a colourless oil (4.4 g, 10.8 mmol, 78%). IR (neat): ν 3060, 3021, 2940, 2863, 2830, 2785, 1595, 1484, 1440, 1305, 1185, 1098, 1026, 950, 738, 695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.57–7.11 (m, 14H, Ar), 4.76 (t, ^3J=7.6 Hz, 1H, CH), 4.05–3.88 (m, 2H, CH_2O), 2.64 (s, 6H, $N(CH_3)_2$), 2.39–2.22 (m, 2H, CH_2), 1.97 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 152.78–120.04 (Ar), 67.86 (d, $^2J_{P,C}$=19.6 Hz, CH_2OP), 45.56 (s, $N(CH_3)_2$), 39.93 (s, CH), 37.80 (d, $^3J_{P,C}$=7.4 Hz, CH_2), 14.38 (s, SCH_3); $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 112.21 (s); ESI MS: *m*/*z* 409 (M^+). Anal. calcd for $C_{24}H_{28}NOPS$: C, 70.39; H, 6.89; N, 3.42. Found: C, 70.63; H, 6.99; N, 3.06.

4.2.5. [1-Methylthio-3-[(diphenylphosphino)oxy]propyl]-benzene (15). Compound **15** was prepared from **13** (2.3 g, 12.6 mmol) by a similar procedure to that described above for **14**, in a yield of 70% (3.2 g, 8.7 mmol), as a colourless oil. IR (neat): ν 3060, 3025, 2945, 2920, 2872, 1594, 1487, 1440, 1228, 1026, 965, 738, 695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.60–7.23 (m, 15H, Ar), 3.99–3.73 (m, 3H, CH and CH_2O), 2.36–2.12 (m, 2H, CH_2), 1.84 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 142.06–127.08 (Ar), 67.52 (d, $^2J_{P,C}$=19.5 Hz, CH_2OP), 47.59 (s, CH), 37.55 (d, $^3J_{P,C}$=7.3 Hz, CH_2), 14.24 (s, SCH_3); $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 112.69 (s). Anal. calcd for $C_{22}H_{23}OPS$: C, 72.11; H, 6.33. Found: C, 72.03; H, 6.25.

4.2.6. Palladium dichloro[2-[(1-methylthio-*S*)-3-[(diphenylphosphino-*P*)oxy]propyl]-*N*,*N*-dimethyl-benzenamine] (16). A solution of the ligand **14** (0.219 g, 0.53 mmol)

in dichloromethane (10 mL) was added dropwise to the dark red solution of $PdCl_2(NCPh)_2$ (0.205 g, 0.53 mmol) in dichloromethane (10 mL) with dry ice/acetone cooling. The reaction mixture was warmed slowly to room temperature and stirred overnight. The resulting yellow–orange solution was evaporated under reduced pressure to a volume of 4 mL, and addition of ether (20 mL) caused the precipitation of a solid. The solvents were decanted and the remaining solid was washed with ether (2×20 mL) and dried, yielding **16** (0.296 g, 0.50 mmol, 95%) as a yellow solid, mp (dec.) 142–145°C. IR (neat): ν 3055, 3020, 2948, 2865, 2830, 2790, 1592, 1485, 1436, 1310, 1187, 1105, 1030, 948, 795, 695 cm^{-1}; ^1H NMR (CD_2Cl_2): δ 8.21–8.14 (m, 2H, Ar), 7.74–7.18 (m, 12H, Ar), 5.11 (br m), 4.78 (br m) and 4.46–4.37 (m) (3×1H, CH and CH_2), 2.45 (s, 6H, $N(CH_3)_2$), 2.56–2.30 (m, obscured with the singlet at 2.45 ppm, 2H, CH_2), 2.20 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ 153.31–121.37 (Ar), 67.96 (CH_2OP), 46.01 ($N(CH_3)_2$), 44.95 (CH), 35.41 (CH_2), 20.93 (SCH_3); $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 119.75 (br s); ESI MS: m/z 552 ($[M-Cl]^+$). Anal. calcd for $C_{24}H_{28}Cl_2NOPPdS$: C, 49.12; H, 4.81; N, 2.39. Found: C, 48.72; H, 4.72; N, 2.01.

4.2.7. Mixture of dimeric palladium species 17 and 18. Treatment of $PdCl_2(NCPh)_2$ (0.222 g, 0.58 mmol) in dichloromethane (10 mL) with ligand **15** (0.212 g, 0.58 mmol) in dichloromethane (15 mL) as described above for the synthesis of **16**, yielded a mixture of the isomeric complexes **17** and **18** as a yellow solid (0.273 g, 0.25 mmol, 86%), mp (dec.) 157–170°C. IR (neat): ν 3060, 2970, 2925, 2885, 1590, 1485, 1440, 1105, 1020, 970, 748, 695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.58–6.88 (m, Ar), 4.50 (br m), 4.20–4.07 (m), 3.65 (br m), 3.22 (br m), 2.89 (br m), 2.59 (br m), 2.29 (s, SCH_3), 1.97 (s, SCH_3) (ratio aromatic–aliphatic protons=15:8); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 131.09–127.69 (Ar), 65.90 (d, $^2J_{P,C}$=9.8 Hz) and 63.64 (s) (CH_2OP), 54.55 (s) and 53.97 (s) (CH), 37.37 (s) and 36.37 (s) (CH_2), 21.39 (s) and 15.24 (s) (SCH_3); $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 113.03 (s) and 111.12 (s). Anal. calcd for $C_{44}H_{46}Cl_4O_2P_2Pd_2S_2$: C, 48.59; H, 4.26. Found: C, 48.50; H, 4.46.

4.3. Crystal structure determination of 16

Crystallographic data for the structure of compound **16** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 189396. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk). Crystal data for **16**: empirical formula, $C_{24}H_{28}Cl_2NOPPdS$; formula weight, 586.80; crystal colour, habit: yellow, prism; crystal dimensions, 0.30×0.35×0.55 mm; lattice parameters, a=17.583(6) Å, b=11.362(4) Å, c=12.567(3) Å; β=91.06(1)°; V=2510.2(3) $Å^3$; space group $P2_1/n$; Z=4; D_{calcd}=1.553 g cm^{-3}; $F(000)$=1192.0; (Mo Kα)=0.71073 Å; residuals, $R1$=0.0241, $wR2$=0.0681.

4.4. Heck reaction

4.4.1. General procedure for the Heck reaction catalysed by complex 16. An oven-dried Schlenk flask, was charged under argon with aryl bromide (1.0 mmol), styrene (0.17 mL, 1.5 mmol), AcONa (0.164 g, 2.0 mmol), a stock solution of complex **14** in DMF (1 or 0.01 mM, 1 mL, 0.001 or 0.00001 mmol, respectively) and decane (0.08 mL, 0.4 mmol) as internal standard, stirred in a preheated 130°C oil bath for 24 h, and then allowed to cool to room temperature. After addition of aqueous NaOH and extraction with dichloromethane, the organic phase was washed with brine, dried over Na_2SO_4, filtered, and analysed by GC and GC-MS. After evaporation of the volatiles, the residue was passed through a pad of silica gel with AcOEt/pentane (5:1) as eluent, dried in vacuo and characterized by GC-MS, ^1H and ^{13}C NMR spectra. All the Heck products are known compounds.[2h,i,4h,j]

4.4.2. General procedure for the Heck reaction catalysed by in situ ligand and $Pd(NCPh)_2$. Aryl bromide (1.0 mmol), styrene (0.17 mL, 1.5 mmol), AcONa (0.164 g, 2.0 mmol), a stock solution of ligand **14** or **15** in DMF (2 or 0.02 mM, 0.5 mL, 0.001 or 0.00001 mmol, respectively), $PdCl_2(PhCN)_2$ in DMF (2 or 0.02 mM, 0.5 mL, 0.001 or 0.00001 mmol, respectively) and decane (0.08 mL, 0.4 mmol) as internal standard, stirred under argon at room temperature for 10 min and then in a preheated 130°C oil bath for 24 h, after which the reaction mixture was allowed to cool to room temperature. The workup procedure was as described above.

Acknowledgements

The investigation was supported by the Greek General Secretariat of Research and Technology and the Russian Foundation for Basic Research.

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