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Aromatic arylation via palladacycles: interception of reaction intermediates

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Dedicated to Professor Fausto Calderazzo in recognition of his outstanding contribution to organometallic chemistry.

Abstract

The palladium-catalysed reaction of iodobenzene with norbornene was carried out in the presence of an excess of methyl acrylate in order to intercept palladium-bonded aryl groups. Species of this kind result from a complex sequence of norbornene insertion into arylpalladium bonds, aromatic substitution and arylation of the palladacycle thus formed, followed by a variety of steps including new norbornene insertion and its eventual expulsion when steric hindrance is generated by the process. © 2000 Elsevier Science S.A. All rights reserved.

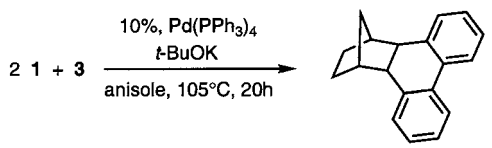
Keywords: Arylation; C–H activation; Heck reactions; Palladacycles

1. Introduction

Some time ago [1] we reported new selective aromatic substitution reactions based on palladium(II) and palladium(IV) promoted multistep sequences involving palladacycle formation and cleavage, for example Scheme 1.

Some of the relevant palladium species involved were isolated and fully characterised. The reaction was later made catalytic by adding a final step (Heck-type reaction) allowing palladium(0) to be formed again [2].

Arylation reactions proved to be much more complex. Depending on conditions they led essentially to three types of products (Eqs. (1)–(3)) [3–5]. The phenyl–norbornyl junction invariably is *exo*.



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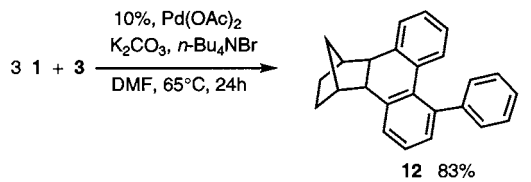

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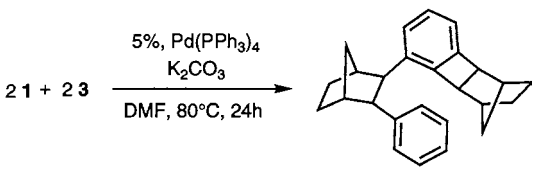

13 52% (3)

Scheme 2 shows the proposed course of the reactions involved. The phenylnorbornyl palladacycle **5** is formed, as shown in Scheme 1, by oxidative addition of phenyl iodide **1** to palladium(0), norbornene insertion into the resulting phenylpalladium bond of **2** and intramolecular aromatic substitution. The attack of a further molecule of **1** occurs on the norbornyl site of the palladacycle **5** and leads to the formation of **14**. Intermediate **14** can give rise to hexahydromethanot-

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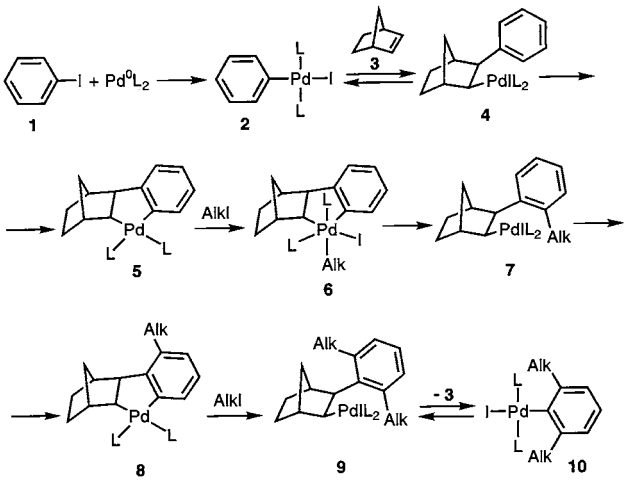
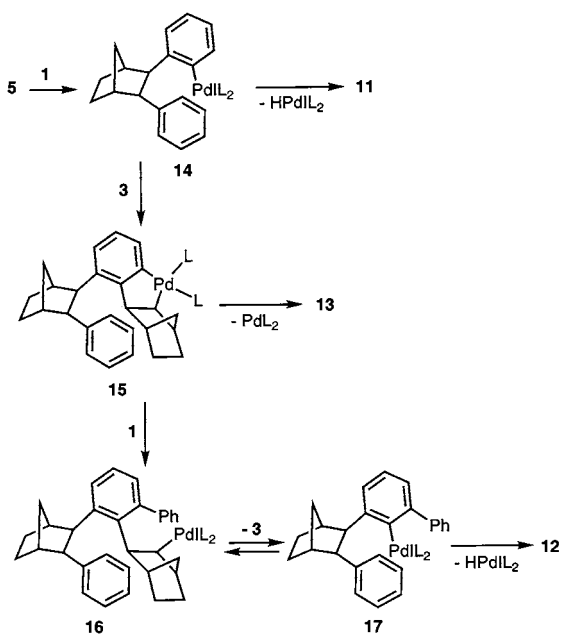


Scheme 1.



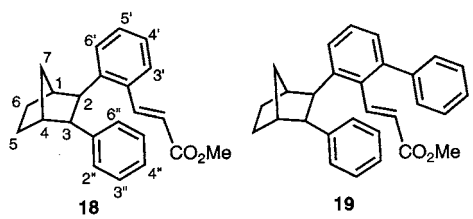
Scheme 2.

riphenylene **11** by aryl–aryl coupling or undergo further reaction through norbornene insertion and intramolecolar aromatic substitution to **15**. Depending on reaction conditions, the new palladacycle **15** can undergo either reductive elimination by ring closure to **13** or further reaction with a third molecule of **1**. As previously shown [6], the presence of a substituent (the arylnorbornyl group) in the position *ortho* to the palladacycle C–C bond induces preferential attack of the aryl group of **1** on the aryl site of the alkylaromatic metallacycle to form **16**. The presence of two substituents in the *ortho* positions then causes norbornene deinsertion [1,2,6], which is followed by ring closure to compound **12**. It is worth noting that in the latter case the second molecule of norbornene is not present in the isolated organic product. In fact it exerts the function of forming a provisional metallacycle **15** (after insertion into the arylpalladium bond), which allows arylation to form compound **16**. The latter spontaneously expels it to give **17**, so that norbornene acts catalytically.

Going through Scheme 2 there are two intermediates, **14** and **17**, that are precursors of hexahydromethanotriphenylene derivatives **11** and **12**, respectively, the latter deriving from the interception of **14** by norbornene. We wondered whether these intermediates could be intercepted by causing them to react with a terminal olefin, thus allowing an easy termination step by β-H elimination, not feasible with a rigid olefin such as norbornene [7]. Achieving such reactions would further confirm the proposed Scheme and in the same time open new synthetic pathways. This is the subject of the present report.

2. Results and discussion

By reacting iodobenzene, norbornene and a ten-fold excess of methyl acrylate in the presence of palladium acetate and potassium carbonate in dimethylformamide (DMF) at 80°C for 18 h, products **18** and **19** were obtained in 27 and 22% yield, respectively. These products are cinnamic esters having unusual bulky substituents in *o*- or *o*,*o*′-positions. Methyl cinnamate, resulting from direct attack of phenylpalladium iodide complex **2** on methyl acrylate, was also formed in 5% yield together with other by-products, each accounting for a few percent, which were not further investigated. Conversion of iodobenzene was 61%.



Compounds **18** and **19** were fully characterised by NMR, IR and mass spectrometry. Assignment of structures is based on COSY, NOESY, 1D-, 2D-TOCSY and decoupling experiments. The NOESY spectra were particularly rich in information. The *exo* substitution of the norbornyl unit is established on the basis of the strong dipolar interaction of the *ortho* protons of the two aromatic rings (H2″, H6″ and H6′) with the bridge proton (H7 *syn*) of the norbornyl unit. This evidence is confirmed by the presence of cross peaks between the *endo* protons H2, H3 and the corresponding *endo* protons H6 and H5. The strong nOe effect between the vinyl proton (=CHAr) and H2 *endo*, clearly indicates

that the acrylic substituent is *ortho* to the norbornyl–aryl junction. Moreover, the second vinyl proton (=$CHCO_2CH_3$) shows nOe interaction only with one aromatic proton (H3′). The *ortho* proton of the doubly substituted ring (H6′) shows cross peaks, with the vicinal H5′, with the H7 *syn* and the corresponding bridgehead proton H1 and not with H2 *endo*. In agreement with this result, the vinyl proton (=CHAr) shows dipolar interaction only with H2 *endo*, thus indicating that rotation around the C (aliphatic)–C (aromatic) bond is restricted and that H6′ is directed towards the same side of the norbornyl bridge, tilted at the bridgehead H1. Further support comes from the nOe interaction of =CHAr with the signals of H2″ and H6″. For compound **19**, the presence of a second substituent (a phenyl moiety) *ortho* to the acrylic chain on the aromatic ring bonded to C2 was confirmed by 1D-TOCSY experiments, which allowed the isolation of a system of three spins from the crowded standard spectrum (Fig. 1) as expected for an aromatic ring containing three adjacent substituents. These data are in agreement with the high-field chemical shift experienced by the vinyl proton =CHAr (from 6.01 to 5.20) and by the dipolar interactions of the latter not only with the two *ortho* protons (H2″, H6″) of the phenyl ring bonded to C3, as in compound **18**, but also with the *ortho* protons (H2‴, H6‴) of the third phenyl ring.

We interpret the course of the reaction leading to **18** and **19** according to Scheme 3. The reaction proceeds up to intermediate **14** as described in the previous Schemes 1 and 2. In place of undergoing ring closure to form the methanotriphenylene derivative **11** (Eq. (1)), complex **14** reacts with the terminal olefin according to a Heck-type reaction [8] to give **18**.

The formation of compound **19** requires a more complex interpretation, which is in accordance with the pathway leading to the formation of compound **12** (Eq. (2)). Complex **14** reacts in part with acrylate, but even in the presence of a large excess of the terminal olefin inserts norbornene and the reaction proceeds, as previously described, to the formation of **17**. Analogously to complex **14**, intermediate **17** undergoes a Heck-type reaction affording **19**. Strained olefins are well known for exhibiting better coordination ability over terminal olefins because of partial strain relief [9]. Norbornene insertion, however, is an equilibrium, which is displaced to the right when it is followed by one or more thermodynamically favourable steps. This step cannot be β-hydrogen elimination, which is stereochemically difficult [7]. Palladacycle **15** formation stabilizes the norbornene insertion and can end up with the irreversible formation of **13** (Eq. (3)). In the presence of an arylating agent, however, palladacycle **15** opens up to allow arylation at the aryl site. As a consequence, the pendant norbornyl-

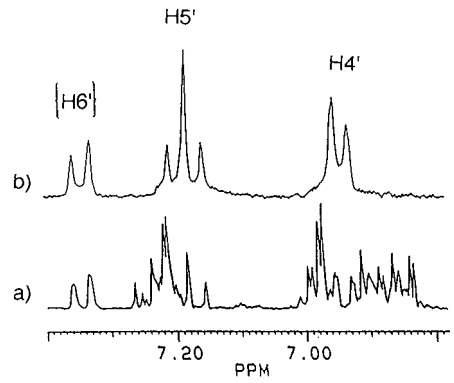
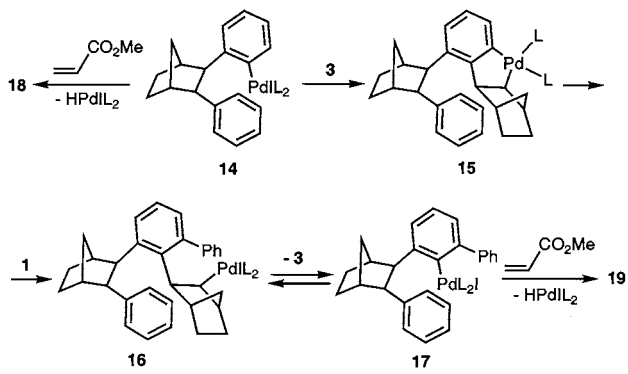


Fig. 1. 300 MHz ^{1}H-NMR spectra of compound **19**: (a) standard 1D spectrum of the aromatic protons; (b) 1D-TOCSY spectrum obtained by selective irradiation of H6′.



Scheme 3.

palladium bond in **16** does not find another way to gain stability and undergoes deinsertion in favour of the insertion of an olefin such as methyl acrylate that can undergo further irreversible step consisting of β-H elimination. In support of this interpretation, we have ascertained that 2,6-di-*ortho*-substituted arylpalladium iodide complexes, unlike the unsubstituted or monosubstituted ones, do not show any tendency to insert norbornene.

The course of the reaction leading to **19** conclusively supports the proposed way for the formation of phenylhexahydromethanotriphenylene **12**. In fact, in the absence of the added olefin the reaction would end up at the level of **12** by ring closure, after trapping of **14** by norbornene and further arylation, as we previously observed, thus excluding an alternative interpretation involving the intermediacy of an aryne [4]. The latter species can intervene in the formation of condensed aromatics [10], but requires quite different conditions.

3. Conclusion

In conclusion, the experiments reported in the present paper are in full agreement with the course

shown in Scheme 2. Furthermore, they extend the scope of the arylation reaction via palladacycles to olefin insertion reactions.

4. Experimental

4.1. General

All reactions were carried out under a nitrogen atmosphere using standard Schlenck techniques. Reagents were commercial grade and were used as obtained. DMF was dried over 4 Å molecular sieves. IR spectra (ν, cm^{-1}) were recorded on a Nicolet 5PC with Fourier transform instrument. Mass spectra were recorded with a Finnigan MAT SSQ10 spectrometer. Elemental analyses were carried out with a Carlo Erba EA 1108 Elemental Analyzer. ^{1}H-NMR spectra were obtained either with a Bruker AMX-400 or a Bruker AM-300. 1D-TOCSY spectra were carried out by a selective inversion obtained by a soft DANTE pulse of about 39.2 ms followed by a MLEV17 for spin-lock used as mixing time (70 ms) [11]. ^{13}C-NMR spectra were obtained with a Bruker AM 300 at 75.5 MHz. All spectra were run in $CDCl_3$ solutions at 293°K using the signal of the solvent (7.26 for ^{1}H and 77.0 for ^{13}C) as reference.

4.2. Reaction of norbornene, iodobenzene and methyl acrylate in the presence of $Pd(OAc)_2$

To a mixture of palladium acetate (32 mg, 0.14 mmol) and potassium carbonate (154 mg, 1.57 mmol) were added iodobenzene (291 mg, 1.42 mmol) and norbornene (161 mg, 1.71 mmol) dissolved in DMF (3 ml) and methyl acrylate (1.5 ml). The resulting solution was stirred at 80°C for 18 h and then treated with CH_2Cl_2, washed with 5% H_2SO_4, dried over sodium Na_2SO_4, filtered and concentrated. The unconverted iodobenzene (113 mg, 39%) was determined by GC quantitative analysis using *n*-dodecane as internal standard. Using flash chromatography (9.5:0.5 hexane–ethyl acetate) the following quantities were eluted: methyl cinnamate (11 mg, 5%), compound **18** (64 mg, 27%) and compound **19** (42 mg, 22%).

4.2.1. exo-2-(2′-(2-E-Methoxycarbonylethenyl)phenyl-3-phenylbicyclo[2.2.1]heptane (**18**)

^{1}H-NMR (400 MHz): δ 7.97 (1H, d, $J = 15.8$ Hz, =CHAr), 7.33 (1H, dd, $J = 7.9$, 1.3 Hz, H6′), 7.22–7.15 (2H, m, H3′, H5′), 6.98 (1H, td, $J = 7.5$, 1.4 Hz, H4′), 6.90–6.85 (3H, m, H3″, H4″, H5″), 6.84–6.80 (2H, m, H2″, H6″), 6.01 (1H, d, $J = 15.8$ Hz, $=CHCO_2CH_3$), 3.84 (3H, s, OCH_3), 3.57 (1H, d, $J = 9.7$ Hz, H2), 3.32 (1H, dd, $J = 9.7$, 1.4 Hz, H3), 2.71 (1H, m, H1), 2.44 (1H, m, H4), 2.32 (1H, d quintets, $J = 10.2$, 2.0 Hz, $H7_{syn}$), 1.88–1.69 (2H, m, $H5_{exo}$, $H6_{exo}$), 1.63–1.50 (3H, m, $H5_{endo}$, $H6_{endo}$, $H7_{anti}$); MS (70 eV): M^+ 332 (25), *m*/*e* 272 (30), 265 (25), 247 (15), 205 (55), 181 (45), 167 (25), 155 (40), 141 (95), 128 (50), 117 (65), 115 (100), 95 (20), 91 (90), 77 (20), 48 (20); FT-IR: 1718, 1632; Anal. Calc. for $C_{23}H_{24}O_2$: C, 83.09; H, 7.28. Found: C, 82.81; H, 7.21%.

4.2.2. exo-2-[2′-(2-E-Methoxycarbonylethenyl)-3′-phenyl]phenyl-3-phenylbicyclo[2.2.1]heptane (**19**)

^{1}H-NMR (400 MHz): δ 7.66 (1H, d, $J = 16.3$ Hz, =C*H*Ar), 7.34 (1H, dd, $J = 8.0$, 1.8 Hz, H6′), 7.26–7.19 (3H, m, H3‴, H4‴, H5‴), 7.18 (1H, t, $J = 7.8$ Hz, H5′), 7.01–6.95 (3H, m, H3″, H4″, H5″), 6.94 (1H, dd, $J =$ 7.6, 1.2 Hz, H4′) 6.92–6.87 (2H, m, H2‴, H6″) 6.87–6.83 (2H, m, H2‴, H6‴) 5.20 (1H, d, $J = 16.2$ Hz, $=CHCO_2CH_3$), 3.68 (3H, s, OCH_3), 3.49 (1H, d, $J = 9.5$ Hz, H2), 3.30 (1H, d, $J = 9.5$ Hz, H3), 2.74 (1H, m, H1), 2.44 (1H, m, H4), 2.35 (1H, d quintets, $J = 10.3$, 1.8 Hz, $H7_{syn}$), 1.84–1.68 (2H, m, $H5_{exo}$, $H6_{exo}$), 1.60–1.40 (3H, m, $H5_{endo}$, $H6_{endo}$, $H7_{anti}$); ^{13}C-NMR: δ 167.1 (CO), 144.9 (q), 144.5 (=*C*HAr), 143.0, 142.5, 141.9, 141.6 (q), 129.4 (C2‴, C6‴), 128.9 (C2″, C6″), 128.0 (C4′), 127.9 (C3‴, C5‴), 127.7 (C5′), 127.2 (C3″, C5″), 126.6 (C4‴), 125.4 (C4″), 124.3 (=*C*HCO_2CH_3), 55.5 (C3), 51.5 (CH_3), 51.0 (C2), 44.2 (C4), 41.0 (C1), 37.3 (C7), 30.9 (C5 or C6), 30.5 (C6 or C5); MS (70 eV): [M^+] 408 (55), *m*/*e* 257 (30), 217 (38), 191 (50), 117 (30), 91 (58), 73 (18), 52 (20), 48 (50); FT-IR: 1718, 1636; Anal. Calc. for $C_{29}H_{28}O_2$: C, 85.25; H, 6.91. Found: C, 84.94; H, 6.88%.

Acknowledgements

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