# Notiz / Note

# Palladium-Catalysed Multiple Coupling Reactions of β-Bromostyrene with Norbornene and Dicyclopentadiene

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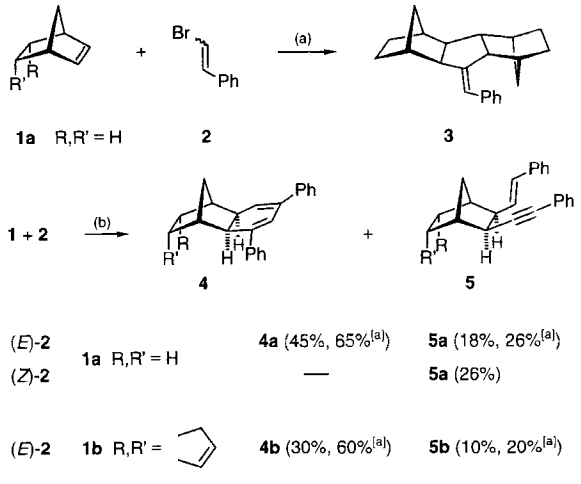
(*E*)-β-Bromostyrene [(*E*)-**2**] reacts with norbornene (**1a**) or dicyclopentadiene (**1b**) in the presence of $Pd(OAc)_2$, $K_2CO_3$, and $n$Bu$_4$NBr in DMF to yield a mixture of the 2:1 coupling products **4** and **5**, while (*Z*)-β-bromostyrene [(*Z*)-**2**] gives exclusively **5**. Under analogous conditions, (*Z*)-3-iodoacrylic acid (**6**) reacts with norbornene (**1a**) to give the diene **11** with an *exo,exo*-2,3-disubstituted norbornane skeleton.

Transition-metal-catalysed carbon–carbon bond forming reactions have steadily been gaining importance for organic synthesis in recent years[1]. Among the most generally applicable methods within this family are the palladium-catalysed Heck-type coupling reactions of alkenes with aryl or alkenyl halides[2]. In our studies on palladium-catalysed sequential coupling processes of various aryl halides to bicyclo[2.2.1]hept-2-ene systems, we have found that the reaction conditions have a remarkable influence on the product distribution[3,4]. The palladium-catalysed coupling of β-bromostyrene (**2**)[5] to norbornene (**1a**) has been reported to produce **3** (79% yield based on converted **2**), when $Pd(PPh_3)_4$ is used as the catalyst, KOAc as the base and anisole as the solvent[6].

We have reinvestigated the coupling of **2** with norbornene (**1a**) under the conditions originally developed by Jeffery[7], i.e. with $Pd(OAc)_2$ as the catalyst precursor, $K_2CO_3$ as the base and $n$Bu$_4$NBr[8] as a phase-transfer catalyst in *N,N*-dimethylformamide (DMF) at 80°C. Independent of the ratio of used starting materials **1a** and (*E*)-**2**, we have not succeeded in detecting the 2:1 coupling product **3** under these conditions. Rather, only the 1:2 products **4a** [45% isolated yield, 65% based on converted (*E*)-**2**] and **5a** [18% isolated yield, 26% based on converted (*E*)-**2**] are formed and easily separated by column chromatography. An analogous 1:2 coupling reaction of **2** is observed with dicyclopentadiene (**1b**) to give **4b** [30% isolated yield, 60% based on converted (*E*)-**2**] and **5b** [10% isolated yield, 20% based on converted (*E*)-**2**]; both products **4b** and **5b** consist of two regioisomers with respect to the position of the double bond in the *endo*-cyclopentene ring. In contrast to (*E*)-**2**, the (*Z*)-configurated β-bromostyrene [(*Z*)-**2**] reacts with norbornene (**1a**) to give **5a** as the only isolable product (26% yield), but with the styrene double bond in the *trans* configuration independent of its configuration in **2**. As in most palladium-catalysed coupling reactions to norbornene (**1a**)[9], all products **4** and **5** have the *exo* configuration with respect to the newly attached substituents.

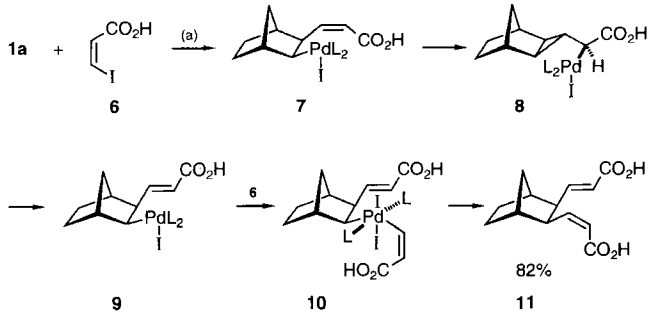
As this domino coupling of an ω-haloalkene appeared to be a rather simple approach to the tri- or tetracyclic hydrocarbon skeleton **4a** or **4b**, respectively, with a 1,3-disubstituted 1,3-cyclohexadiene fragment, (*Z*)-3-iodoacrylic acid (**6**) has been treated with **1a** as well. Surprisingly, this coupling reaction does not yield any product with a cyclohexadiene unit but the *exo,exo*-2,3-disubstituted norbornane derivative **11** with one (*E*)- and one (*Z*)-configurated acrylic acid unit.

Scheme 1. (a) $Pd(PPh_3)_4$, KOAc, anisole, 60°C. – (b) $Pd(OAc)_2$, $K_2CO_3$, $n$Bu$_4$NBr, DMF, 80°C




[a] Yield based on converted (*E*)-**2**.

Scheme 2. (a) $Pd(OAc)_2$, $NaHCO_3$, DMF, 70°C

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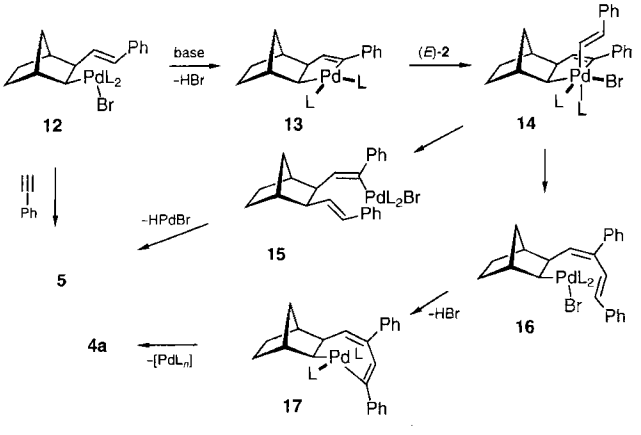
The (*E*) configuration of one acrylic acid unit in **11** can be rationalised by assuming the formation of a cyclopropylmethylpalladium iodide intermediate **8** from the adduct **7** of the first organopalladium intermediate formed from **6** and **1a** and subsequent ring opening to give the thermodynamically more stable (*E*)-configurated intermediate **9** in accord with literature precedence[10]. Apparently, **9** must be able to undergo another oxidative addition of an iodoacrylic acid molecule **6** to give a palladium(IV) intermediate **10**[11], which upon reductive elimination yields **11**.

In contrast to this it must be assumed that the intermediate **12** formed by *syn* addition of (*E*)-styrylpalladium bromide to the double bond in **1a**, in analogy to the mechanism for the coupling of iodobenzene to **1a**[3a,12], can be dehydrobrominated to the palladacyclopentene **13**, which can oxidatively add another equivalent of **2** to give the intermediate **14** with octahedrally coordinated palladium(IV)[11]. Insertion of the newly attached styryl unit into one of the Pd–C bonds produces either **15** or **16**. However, the cyclohexadiene **4** can only be formed from **16** via the palladacycloheptadiene **17** by reductive elimination of the catalytically active palladium species. On the other hand, the intermediate can undergo elimination of HPdBr to give the alkynyl derivative **5**. Compound **5** is exclusively formed when (*Z*)-**2** is employed instead of (*E*)-**2**. This can be rationalized with a second pathway, along which *cis* elimination of HPdBr occurs from the first intermediate (*Z*)-(2-phenylethenyl)palladium bromide generating phenylacetylene, which is known to couple with the palladium intermediate **12**[13]. As *cis-trans* isomerisations of alkenes readily take place in the presence of a palladium catalyst[14], formation of phenylacetylene and its coupling to give **5** can also occur as a side reaction with (*E*)-**2**.

It is not at all understood, however, why (*Z*)-3-iodoacrylic acid (**6**) yields the *exo,exo*-2,3-disubstituted norbornane **11** exclusively.

Scheme 3




In conclusion, the sequential palladium-catalysed coupling reaction of (*E*)-**2** to **1** offers a simple approach to the tricyclic and tetracyclic carbon skeletons **4a** and **4b**, respectively. This result once again demonstrates that Heck-type reactions of norbornene and norbornene derivatives are particularly sensitive to the nature of the palladium catalyst and the reaction medium.

## Experimental

All operations were performed under $N_2$; solvents were dried by distillation from sodium or potassium/benzophenone. – $^1$H NMR: Varian XL 200 (200 MHz), VXR-500S (500 MHz), Bruker AM 250 (250 MHz), AX 300 (300 MHz). – $^{13}$C NMR: Varian XL 200 (50.3 MHz); multiplicities were determined by APT (Attached Proton Test) measurements; chemical shifts refer to $\delta_{TMS} = 0.00$ according to the chemical shifts of residual solvent signals. – IR: Bruker IFS 66, Perkin-Elmer 298. – MS: Varian MAT 311A, Finnigan MAT 95. – HRMS: Varian MAT 311A. – Melting points (uncorrected): Büchi 510. – Elemental analysis: Mikroanalytisches Laboratorium des Instituts für Organische Chemie der Georg-August-Universität Göttingen.

*General Procedure (GP) for the Palladium-Catalysed Coupling Reactions:* A mixture of $K_2CO_3$ (1.96 g, 14.2 mmol), $n$Bu$_4$NBr (1.93 g, 6.0 mmol) and $Pd(OAc)_2$ (54 mg, 0.24 mmol) in *N,N*-dimethylformamide (DMF) (20 ml) was heated to 60°C for 30 min under $N_2$. Afterwards, a solution of the alkene **1** (5.0 mmol) and β-bromostyrene (**2**) (1.91 g, 10.4 mmol) in DMF (20 ml) was added with stirring over a period of 12 h, and the mixture was stirred for an additional 12 h at 80°C. After the mixture had been cooled to room temp., *tert*-butyl methyl ether (60 ml) was added and the precipitate filtered off. The organic solution was extracted with $H_2O$ (3 × 30 ml), dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was separated by chromatography on silica gel with petroleum ether as eluent.

*3,5-Diphenyltricyclo[6.2.1.0$^{2,7}$]undeca-3,5-diene* (**4a**): According to the GP, norbornene (**1a**) (470 mg, 5 mmol) gave 670 mg [45%, 65% based on converted (*E*)-**2**] of **4a** ($R_f = 0.36$) as colourless crystals, m.p. 75°C. – IR (KBr): $\tilde{\nu}$ = 3070 cm$^{-1}$, 3040, 2960, 2875, 1610, 1495, 1450, 710. – $^1$H NMR (250 MHz, $CDCl_3$): δ = 1.02–1.69 (m, 6H, alkyl-H), 2.11 (br. s, 1H, 1- or 8-H), 2.25 (br. s, 1H, 8- or 1-H), 2.93 (d, $^3J$ = 6.0 Hz, 1H, 2-H), 3.14 (dd, $^3J$ = 6.0, $^3J$ = 1.8 Hz, 1H, 7-H), 6.00 (d, $^3J$ = 1.8 Hz, 1H, 6-H), 6.46 (s, 1H, 4-H), 6.78–7.24 (m, 10H, phenyl H). – $^{13}$C NMR (50.3 MHz + APT, $CDCl_3$): δ = 28.55 (–), 29.75 (–), 31.83 (–), 39.87 (+), 44.81 (+), 52.35 (+), 54.33 (+), 120.68 (+), 125.11 (+), 126.13 (+), 126.68 (+), 127.14 (+), 127.63 (+), 128.94 (+), 137.52 (–), 137.99 (–), 144.07 (+), 147.86 (–), 148.73 (–). – MS (70 eV); *m/z* (%): 298 (54) [M$^+$], 202 (100), 180 (80), 179 (95), 178 (95), 165 (58), 132 (36), 105 (38). – $C_{23}H_{22}$ (298.4): calcd. C 92.57, H 7.43; found C 92.51, H 7.38. – In addition, 268 mg [18%, 26% based on converted (*E*)-**2**] of *exo-2-(Phenylethynyl)-exo-3-[(E)-2-phenylethenyl]norbornane* (**5a**) ($R_f = 0.09$) was isolated as a colourless oil. The spectroscopic data are in agreement with those reported in the literature[13b].

*endo-9,10-Cyclopenteno-3,5-diphenyltricyclo[6.2.1.0$^{2,7}$]undeca-3,5-diene* (**4b**): According to the GP, dicyclopentadiene (**1b**) (660 mg, 5 mmol) gave 504 mg [30%, 60% based on converted (*E*)-**2**] of **4b** as a colourless oil, mixture of two regioisomers with respect to the double bond in the cyclopentene unit ($R_f = 0.24$). – IR (KBr): $\tilde{\nu}$ = 3075 cm$^{-1}$, 3037, 2964, 2917, 2876, 1618, 1491, 1460, 1355, 1156, 870, 832. – $^1$H NMR (250 MHz, $CDCl_3$): δ = 1.54 [AB system, $\delta_A = 1.32$, $\delta_B = 1.82$, $^2J$ = 14.0 Hz, 2H, 11(11')-H], 2.08–2.65 (m, 4H), 2.73–3.36 (m, 4H), 5.78–5.98 (m, 2H), 6.08 (br. s, 1H, 6-H), 6.53 (s, 1H, 4-H), 6.75–7.81 (m, 10H, phenyl H). – $^{13}$C NMR (50.3 MHz, $CDCl_3$): δ = 32.16 (–), 32.29 (–), 34.93 (–), 35.11 (–), 42.02 (+), 42.45 (+), 42.94 (+), 44.46 (+), 44.69 (+), 46.54 (+), 47.62 (+), 47.85 (+), 49.65 (+), 49.79 (+), 52.84 (+), 53.94 (+), 119.99 (+), 120.26 (+), 125.03 (+), 125.04 (+), 126.04 (+), 126.49 (+), 126.63 (+), 127.11 (+), 127.59 (+), 128.63 (+), 128.91 (+), 130.89 (+), 131.33 (+), 132.05 (+), 132.14 (+), 137.41 (–), 137.72 (–), 138.92 (–), 139.86 (–), 144.58 (+), 144.91 (+), 147.52 (–), 148.41 (–), 149.36 (–), 149.53 (–). – MS (70 eV); *m/z* (%): 336 (10) [M$^+$], 278 (13), 262 (14), 105 (100), 91 (30), 77 (48). – $C_{26}H_{24}$ (336.5): calcd. C 92.81, H 7.19; found C 92.43, H 7.56. – As a second product 168 mg [10%, 20% based on con-

verted (*E*)-**2**] of *exo/endo-9,10-Cyclopenteno-exo-2-phenylethynyl-exo-3-[(E)-2-phenylethenyl]norbornane* (**5b**) was isolated as a colourless oil, mixture of two regioisomers ($R_f$ = 0.17). – $^1$H NMR (250 MHz, [D$_6$]benzene): δ = 1.21–1.35 (m, 1H), 1.95–3.12 (m, 9H), 5.32–5.55 (m, 2H, alkene H), 6.40 (dd, $^3J$ = 16.0, $^3J$ = 9.0 Hz, 1H), 6.54 (d, $^3J$ = 9.0 Hz, 1H), 6.91–7.17 (m, 6H), 7.39–7.43 (m, 4H). – $^{13}$C NMR (50.3 MHz, $CDCl_3$): δ = 26.96, 32.24, 32.95, 35.89, 37.84, 41.39, 41.84, 42.07, 44.46, 46.04, 47.35, 48.94, 49.42, 52.30, 52.80, 83.28, 83.51, 92.21, 92.29, 124.09, 126.07, 126.47, 126.73, 127.27, 127.58, 128.06, 128.39, 128.64, 128.72, 129.02, 131.31, 131.44, 131.74, 131.83, 132.14, 133.38, 133.53, 138.00. – $C_{26}H_{24}$: calcd. 336.1078, found 336.1078 ± 0.0002 (MS).

*Bicyclo[2.2.1]heptane-exo,exo-2,3-diylbis[(E/Z)-acrylic Acid]* (**11**): A mixture of **1a** (500 mg, 5.3 mmol), **6** (2.14 g, 10.8 mmol), $NaHCO_3$ (2.52 g, 30.0 mmol), and $Pd(OAc)_2$ (24 mg, 0.11 mmol) in DMF (20 ml) was heated at 70°C in a closed screw-capped Pyrex bottle for 12 h under $N_2$. After the reaction mixture had been cooled to room temp., 50 ml of $CH_2Cl_2$ was added, the solids were separated by filtration, and the organic phase was extracted with 2 N HCl (4 × 20 ml). The organic layer was dried with $MgSO_4$, and the solvents were evaporated under reduced pressure. The resulting oil weighed 1.02 g (82%) and was slightly impure **11**. An analytically pure sample was obtained by crystallisation from *tert*-butyl methyl ether as colourless crystals, m.p. 138°C. – IR (KBr): $\tilde{\nu}$ = 3350 cm$^{-1}$, 2950, 1680, 1630, 1452, 1282, 1252. – $^1$H NMR (500 MHz, $CDCl_3$): δ = 1.22 (d, $^2J$ = 10.6 Hz, 1 H, 7-H), 1.29 [dd, $^2J$ = 10.0, $^3J$ = 3.0 Hz, 2 H, 5(6)-H$_{endo}$], 1.55 [ddd, $^2J$ = 10.0, $^3J$ = 10.0, $^3J$ = 3.0 Hz, 2 H, 5(6)-H$_{exo}$], 1.62 (d, $^2J$ = 10.6 Hz, 1 H, 7-H), 2.05 (s, 1 H, 1- or 4-H), 2.17 (s, 1 H, 4- or 1-H), 2.66 (dd, $^3J$ = 9.5, $^3J$ = 9.5 Hz, 1 H, 2- or 3-H), 3.48 (dd, $^3J$ = 9.8, $^3J$ = 9.6 Hz, 1 H, 3- or 2-H), 5.67 (d, $^3J$ = 15.5 Hz, 1 H, alkenyl H), 5.71 (d, $^3J$ = 11.4 Hz, 1 H, alkenyl H), 6.00 (dd, $^3J$ = 11.4, $^3J$ = 10.0 Hz, 1 H, alkenyl H), 6.66 (dd, $^3J$ = 15.5, $^3J$ = 9.5 Hz, 1 H, alkenyl H). – $^{13}$C NMR (50.3 MHz, $CDCl_3$): δ = 28.78 (–), 28.98 (–), 34.29 (–), 41.00 (+), 42.84 (+), 46.96 (+), 50.70 (+), 119.39 (+), 119.84 (+), 152.62 (+), 153.03 (+), 171.26 (–), 171.82 (–). – MS (70 eV); *m/z* (%): 236 (3) [M$^+$], 218 (100), 190 (26), 173 (42). – $C_{13}H_{16}O_4$ (236.3): calcd. C 66.09, H 6.83; found C 66.57, H 6.28.

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