Palladium-catalyzed, stereoselective rearrangement of a tetracyclic allyl cyclopropane under arylation†

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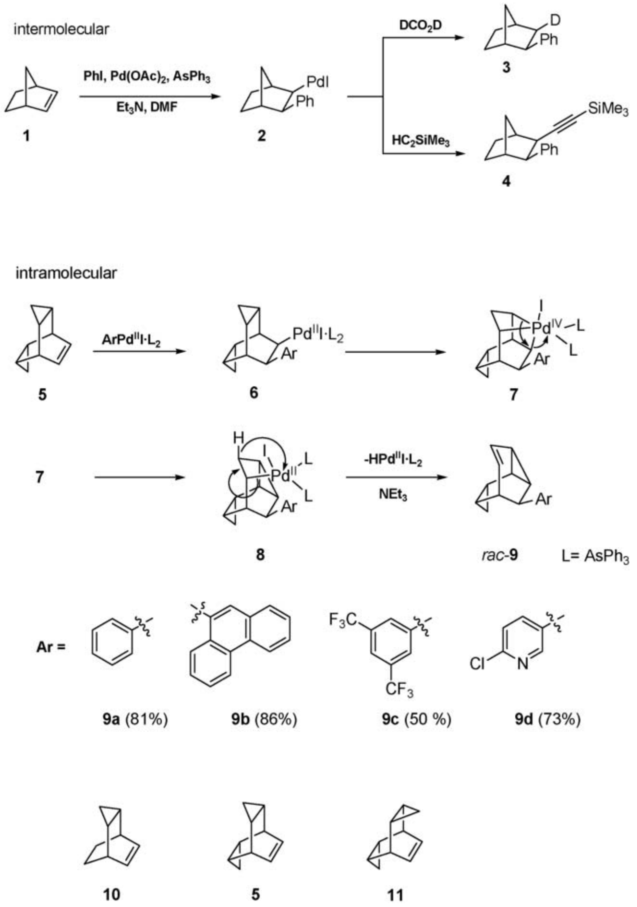
The first example of a π,σ domino-Heck reaction under concomitant rearrangement of the tetracyclic allylcyclopropane *endo*,*exo*-bishomobarrelene (5) is reported; the stereoselective reaction proceeds *via* an intramolecular insertion of a primarily-formed carbopalladation intermediate into a strained cyclopropane C–C σ-bond, giving 9.

Since their discovery by R. F. Heck in 1972,[1] palladium-catalyzed arylations of acyclic and cyclic alkenes have gained increasing synthetic importance, clearly demonstrated by the impressive number of more than 2500 articles published so far in different fields of application.[2] Starting with bicyclic alkenes such as norbornene (**1**) (Scheme 1), the final *syn*-dehydropalladation of the carbopalladation intermediate **2** is no longer feasible because of the rigid molecular geometry; **2** can react further intermolecularly instead, *e.g.* under reduction by formate or deuterioformate, respectively, to **3**, or with C-nucleophiles such as trimethylsilylacetylene to **4**.[3] Both the carbopalladation and the consecutive substitution reactions proceed with complete *exo*-diastereoselectivity. Inter- or intramolecular sequential insertion reactions of a carbopalladation product into a strained cyclopropane C–C σ-bond are still unknown. To test this possibility, the hydroarylation of the easily accessible *endo*,*exo*-bishomobarrelene (**5**)[4] was investigated. **5** represents a *cis*-allylcyclopropane model compound which can be attacked from one side only due to shielding by the second cyclopropane ring.

Treatment of **5** with iodobenzene under the optimized hydroarylation conditions for bicyclic alkenes (Pd(OAc)$_2$, AsPh$_3$, NEt$_3$, HCO$_2$H, DMF, 65 °C)[5–7] surprisingly led to the formation of 9-phenylbishomosemibullvalene (rac-**9a**)[8] in 81% yield; a hydroarylation product was not even formed in traces. This palladium-catalyzed phenylation of an allylcyclopropane unit under sequential rearrangement of a (cyclopropylethyl)palladium subunit into a new one of the same type is novel, and may be classified as the first example of a π,σ domino-Heck reaction under concomitant skeletal rearrangement. The tetracyclic structure of **9a** was first assigned on the basis of its ^{1}H- and ^{13}C-NMR as well as its mass spectra.[9] The relative configuration of **9a** was finally proven by an X-ray crystal structure analysis‡ of its well-crystallizing derivative **9b** (Fig. 1), synthesized analogously through palladium-catalyzed coupling with 9-iodo-phenanthrene (86% yield).[10,11]



Scheme 1 Inter- and intramolecular sequential reactions of the bicyclic carbopalladation products **2** and **6**.

In *exo*,*exo*-bishomobarrelene (**11**), which is isomeric to **5**, the double bond is shielded on both sides meaning that such an addition is not feasible any longer.

The transformation of **5** is supposed to start with the *syn*-addition of a preformed ArPdI species to the C=C double bond, giving **6**. The sequential reaction steps can then proceed *via* different mechanistic pathways. Firstly, because of its vicinity to the Walsh orbitals of the *endo*-cyclopropane ring, the palladium(II) substituent should be able to first interact and then finally insert into the strained cyclopropane σ-bond under oxidation, giving the

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† Palladium-catalyzed reactions part 5; For part 4 see ref. 7.

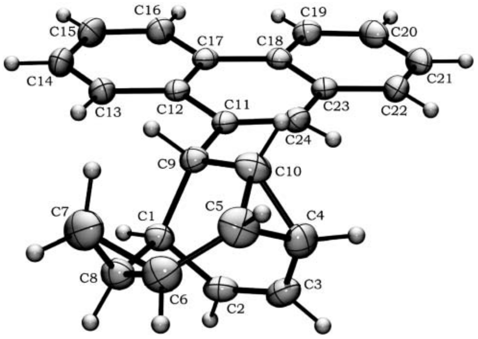

Fig. 1 X-Ray crystal structure of **9b**.

Pd(IV) species **7**. This highly strained octahedral complex[12] could then stabilize itself by a reductive elimination under concomitant rearrangement to give the σ-alkyl-palladium(II) complex **8**. Due to model type considerations, rearrangement to the new (2-cyclopropylethyl)palladium derivative **8** should be more favored energetically in comparison to an alternative formation of a more strained tetracyclic cyclobutylethyl derivative. Complex **8** has the structural prerequisites for a final *syn*-elimination of hydrido-palladium iodide under formation of the final product **9**. Alternatively, the reaction could also proceed through σ-bond metathesis between a C–Pd bond and a cyclopropane C–C σ-bond.

Additional experimental findings support the first step of the proposed mechanism of this domino reaction. While bromobenzene still reacted very slowly under these reaction conditions, the electron deficient (hetero)aromatic compounds 1-iodo-3,5-bis(trifluoromethyl)benzene and 3-iodo-6-chloro-pyridine could also be converted in good yields (50, 73%) into the 9-arylsemibullvalene derivatives **9c** and **9d**, respectively. In addition to triphenylarsine, triphenylphosphine and the bidentate bisphosphine rac-BINAP also proved to be both activating and stabilizing ligands. Under hydroarylation conditions with iodobenzene, the best yield was obtained (81%). Without triethylamine as a base, the product yield dropped strongly, and without both a base and a ligand, **9a** was formed in trace quantities only. In the presence of palladium(II) acetate/triphenylarsine or tetrakis(triphenylphosphine)palladium(0) without concomitant addition of iodobenzene, no reaction occurred. Transition metal-catalyzed, cationic rearrangements of numerous polycyclic small-ring compounds are known from the literature for copper(I), silver(I), gold(I), rhodium(I) and palladium(II) salts,[13] but only without aryl concomitant substitution.

Starting with **10** as the structural key compound, activation through achiral ligands such as triphenylphosphine or triphenylarsine naturally resulted in the formation of the phenylated rearrangement products of **10** in a racemic form. When, in a first experiment, the chiral bisphosphine (*R*)-BINAP was used instead in an enantiomerically pure form under identical reaction conditions, the product was already obtained with an enantiomeric excess of 15%. During this novel asymmetric C–C coupling reaction under rearrangement, five chiral centers were controlled in a single operation! Detection of the enantiomeric excess proved difficult, but was finally achieved by analytical GC separation on a fused silica capillary column with a chemically-bonded chiral phase (octakis-(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin).

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9 *Typical experimental procedure*: A solution of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and $AsPh_3$ (33.7 mg, 0.11 mmol) in dry DMF (3 mL) was stirred in a Schlenk flask under nitrogen at 65 °C for 15 min in order to form the catalyst complex. Then iodobenzene (306 mg, 1.5 mmol), bishomobarrelene **5** (132 mg, 1.00 mmol), triethylamine (354 mg, 3.5 mmol) and formic acid (138 mg, 3.0 mmol) were added. The mixture was heated to 65 °C for 15 h. After cooling down to rt, brine (50 mL) was added, the reaction mixture was extracted with diethyl ether and dried over $MgSO_4$. The solvent was evaporated, the residue purified by chromatography (30 g flash-silica gel, pentane, $R_F = 0.47$): 168 mg (81%). 9-Phenyltetracyclo[3.3.2.$0^{6,8}$.$0^{4,10}$]dec-2-ene (**9a**): colourless, viscous oil. ^{1}H-NMR (400 MHz, $CDCl_3$): $\delta = 0.22$ (ddd, $J = 8.2$, 7.9 and 5.1 Hz, 1 H, 7-H), 0.46 (ddd, $J = 5.1$, 5.0 and 4.1 Hz, 1 H, 7-H), 1.01 (dddd, $J = 12.7$, 7.9, 4.1 and 3.2 Hz, 1 H, 6-H), 1.16 (dddd, $J = 12.7$, 8.2, 6.1 and 5.0 Hz, 1 H, 8-H), 1.44 (dddd, $J = 8.0$, 8.0, 2.2 and 2.0 Hz, 1 H, 10-H), 1.63 (ddd, $J = 8.0$, 8.0 and 3.2 Hz, 1 H, 5-H), 1.72 (ddd, $J = 8.0$, 8.0 and 6.6 Hz, 1 H, 4-H), 2.68 (ddd, $J = 6.4$, 6.1 and 2.2 Hz, 1 H, 1-H), 3.22 (br. s, 1 H, 9-H), 5.67 (dd, $J = 9.3$ and 6.4 Hz, 1 H, 2-H_{olefin}), 6.05 (dd, $J = 9.3$ and 6.6 Hz, 1 H, 3-H_{olefin}), 7.14–7.18 (m, 1 H, H_{aryl}) and 7.23–7.25 (m, 4 H, H_{aryl}); ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 0.8$ (C-7), 7.0 (C-6), 15.4 (C-8), 18.3 (C-4), 19.0 (C-5), 19.4 (C-10), 33.5 (C-9), 37.2 (C-1), 125.8 (C_{aryl}-4′), 126.0 (C_{olefin}-3), 127.7 (2C, C-3′ and C-5′), 128.2 (2C, C-2′ and C-6′), 129.6 (C_{olefin}-2) and 144.0 (C-1′); MS (EI, 70 eV): *m*/*z* (%) = 208 (30) [M^+], 193 (14), 178 (10), 165 (32), 154 (29), 142 (17), 130 (34), 117 (100), 104 (16) [Ph-$C_2H_3^+$], 91 (40) [$C_7H_7^+$] and 77 (19) [$C_6H_5^+$]; HRMS: $C_{16}H_{16}$ requires 208.2982; found 208.2982.

10 9-(9-Phenanthryl)tetracyclo[3.3.2.$0^{6,8}$.$0^{4,10}$]dec-2-ene, $C_{24}H_{20}$, colourless crystals, mp. 154–156 °C (from *n*-hexane), $M_r = 308.42$. Crystal data for **9b**: $C_{48}H_{40}$, $M = 616.8$, monoclinic *C*-centered, space group *C*2/*c* (no. 15), $a = 22.183(7)$, $b = 6.6592(12)$, $c = 22.362(6)$ Å, $\beta = 92.17(2)°$, $V = 3300.9(14)$ Å^3, $Z = 4$, $\mu = 0.070$ mm^{-1}, $D_{x.} = 1.241$ mg m^{-3}, $F(000) = 1312$. 10340 (2500 unique) reflections (θ range 2.54–23.99°) with $R_{int} = 0.0594$ were measured on a Stoe IPDS I diffractometer (λ (Mo-Kα) = 0.71073 Å) with an Oxford Cryostream Cooler Device ($T = 223(2)$ K). Refinement of 297 parameters on F^2 using SHELXL-97[11] resulted in $R1 = 0.0304$ and $wR2 = 0.0595$ for 1352 reflections, and with $I > 2\sigma(I)$ $R1 = 0.0728$, $wR2 = 0.0679$ and goodness-of-fit = 0.987 for all reflections. Maximum/minimum residual electron density in the final difference map was 0.10/−0.09e Å^{-3}, respectively‡.

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