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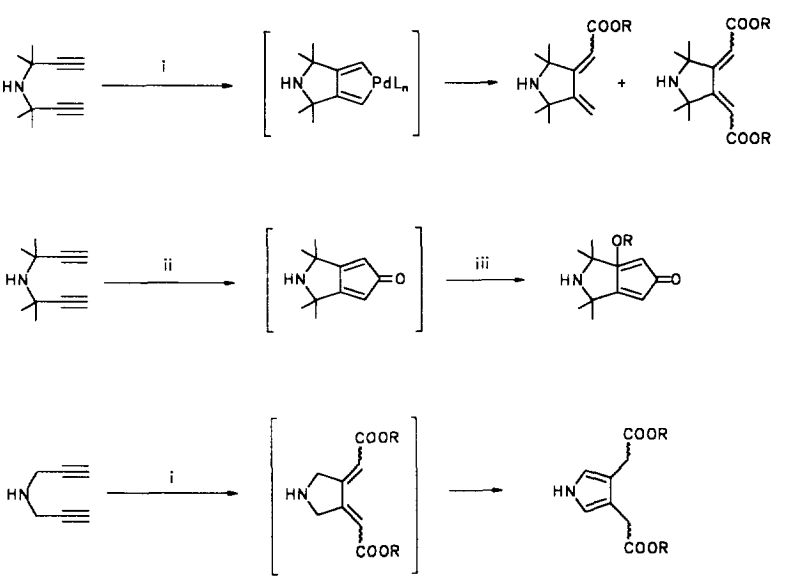
The Palladium Mediated Conversion of 1,6-Diazacyclodeca-3,8-diynes to 3,3'-Bispyrroles. An Unexpected Reorganization of an Alkyne π-System.

Rolf Gleiter* and Joachim Ritter
Organisch-Chemisches Institut der Universität Heidelberg,
Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany.

Abstract: The Pd-catalyzed rearrangement of 1,6-diisopropyl-1,6-diazacyclodeca-3,8-diyne (**1b**) to N,N'-diisopropyl-3,3'-bispyrrole (**2b**) in a one pot reaction involves forming two new C-C bonds, cleaving one triple bond, two allylic rearrangements and two dehydrogenation steps.

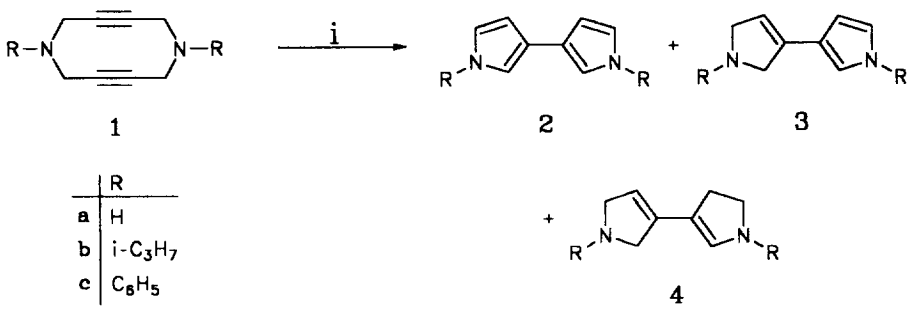
The reaction of bispropargyl-substituted amines with transition metal compounds results in rearrangement (reorganization) of the π-system[1-4]. In aprotic solvents trimerization or tetra-



Scheme 1. Reagents and conditions: i, 10% Pd/C, CH_3OH, KI, CO/O_2; ii, 10% Pd/C, CO, CH_2OH; iii, ROH, NaOH.

merization of the triple bonds[2] is usually observed. The catalytic cotrimerization with CO to the corresponding cyclopentadienones has also been formulated. When performed in alcohols in the presence of CO, transannular coupling to cis-butadiene derivatives with CO insertion occurs. In those cases where the α-positions to the amino group are not fully alkylated the formation of pyrrole derivatives is observed. These observations may be explained via the formation of a metallacycle as an intermediate which, depending on the cosubstrate (e.g. CO, O_2, CH_3OH), affords the corresponding insertion product (Scheme 1).[1-3]

These results and the observation that medium-sized cyclic diynes very often differ[5] in their reactivity from the open chain congeneres led us to react 1,6-diazacyclodeca-3,8-diynes[6] with catalytic amounts of Pd/C. In Scheme 2 and Table 1 the results are summarized for 1,6-diisopropyl-1,6-diazacyclodeca-1,6-diyne (**1b**).



Scheme 2. Reagents and conditions: i, 5% Pd/C, CH_3OH, 80 - 140 °C.

Heating **1b** in methanol (Ar atmosphere, oxygen free solvent) to 140°C with catalytic amounts of (5%)-Pd/C for 2 - 2.5 h affords in nearly quantitative yield the 3,3'-bispyrrole **2b**. At lower temperatures (Table 1) the yield of **2b** is decreased in favor of the dihydro- (**3b**) and the

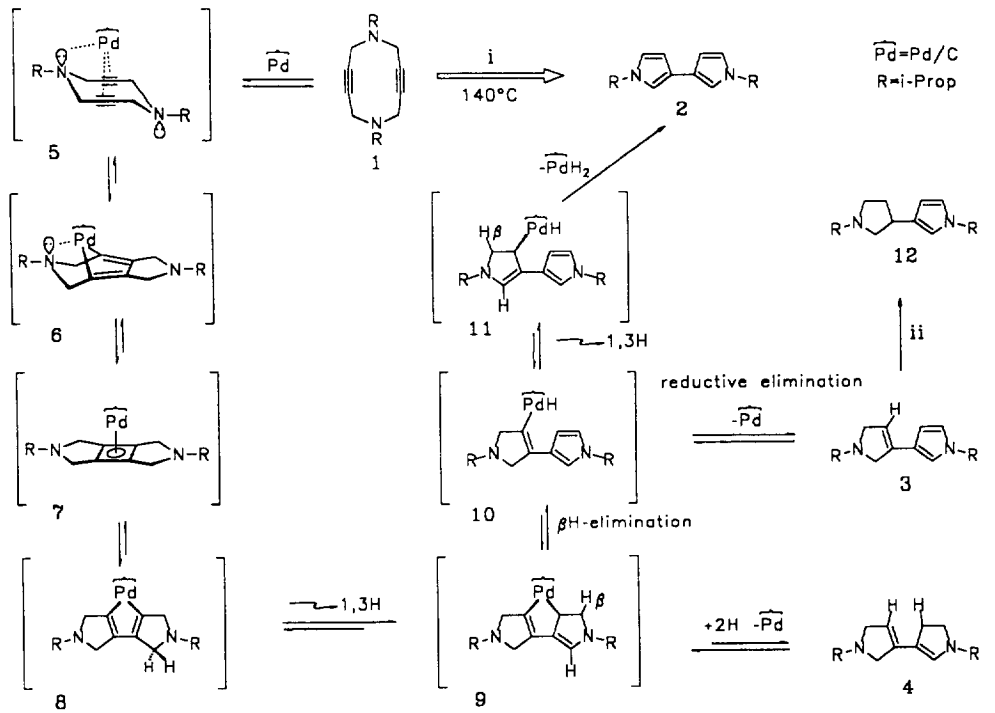
Table 1. Yields of **2** - **4** as a function of the temperature

		yields [%]		
T [°C]	t [h]	**2b**	**3b**	**4b**
140	2	95	0 - 5	< 1
120	1.5	45	40	10 - 15
100	3	10 - 15	45	40
85	14	35	45	20

tetrahydro- (**4b**) derivatives.The structural assignment of the products is based on NMR-and HRMS spectra.[7] When **1b** reacted in CD_3OD, no incorporation of deuterium into the product is observed. The reaction time is also unaffected. This implies that the protons of the solvent molecules are not involved in the reaction.This type of cyclic cascade carbopalladation[8] reaction

may also be performed with **1a** and **1c** to give the corresponding 3,3-bispyrroles **2a**[9] and **2c**, respectively. However, the yields are lower for **2a** and **2c** (ca. 50%) than for **2b** (95%).

To rationalize the reaction sequence we assume that the surface Pd atoms coordinate in an out-of-plane fashion (**5**, Scheme 3). This coordination should be supported by the nitrogen lone-pair(s) as shown in Scheme 3. The next step of the proposed reaction mechanism is the formation of the metallacycles **6** and **8**, whereas the latter should be more favored than **6** for steric reasons. This sequence is consistent with the formation of two new C-C bonds and, in the case of **8**, the cleavage of the former C-C triple bond[11]. The metallacycle **8** is the key intermediate to rationalize the pyrrole rings. The generation of the pyrrole rings from **8** involves first an isomerization of the double bonds. For this process, several mechanisms are discussed in the



Scheme 3. Reagents and conditions: i, 5% Pd/C, CD_3OD, 140 °C; ii, H_2 (50 bar), 90 °C, Pd/C.

literature[10] which should lead to the intermediates **9** - **11** (Scheme 3). The product **3**, which could be isolated at lower temperatures, is most likely formed via reductive elimination from the Pd center in **10**. Heating the product mixtures formed at lower temperatures to 140°C again gives 90 - 95% **2b** indicating that the formation of **3** and **4** from the proposed intermediates **9** and **10** should be reversible. The structural assignement of **3** is supported by its formation to **12b** additionally. A further product observed at lower temperatures, **4b**, can be rationalized via hydrogenolyses of **9** by the hydrogen absorbed at the metal.

There are two major points of interest: i) the experiments carried out at lower temperatures (85 to 120°C) show that the activation energy of the Pd-catalyzed rearrangement of the π-system of **1** to

2 requires less activation energy than the transannular addition of CH_3OH to **1**[12]; ii) higher temperature (140°C) is required for the isomerization of the double bonds and the dehydrogenation steps.

It is also remarkable that from this class of compounds, only **2a** has been prepared previously in a low yield multistep reaction sequence[9]. The cascade of reactions proposed in Scheme 3 is not only mechanistically interesting but also provides an efficient synthetic route to 3,3'-bispyrroles.

Experimental Section

Materials and Methods. All manipulations were carried out under argon. The solvents used (methanol) were dried and distilled under argon. ^1H and ^{13}C NMR spectra were recorded at 300 and 75.46 MHz, respectively, in $CDCl_3$.

Thermolysis of 1,6-diisopropyl-1,6-diazacyclodeca-3,8-diyne (1b) in presence of catalytic amounts of palladium at 140 °C. A solution of 436 mg (2 mmol) of 1,6-diisopropyl-1,6-diazacyclodeca-3,8-diyne in 110 ml of methanol was heated under stirring with 10 mg (0.003 mmol) of palladium metal (10%, Pd/C) at 140 ° C for 2 h in an autoclave under argon. The pressure was recorded to be 15 bar. After 2 h the red solution was filtered under argon and the solvent removed in vacuum. Kugelrohrdistillation at 130 °C / 0.01 torr yields 350 mg (81%) of N,N-diisopropyl-3,3'-bispyrrole (**2b**) as a yellow oil which solidifies. **2b**: ^1H NMR δ: 6.80, 6.66, 6.23 (AA'BB'CC', 3 x m, each 2 H), 4.20 (hept., ^3J = 6.7 Hz, 2 H), 1.45 (d, ^3J = 6.7 Hz, 12 H). ^{13}C NMR δ: 119.6 (s, =C-), 118.4, 113.6, 105.6 (3 x d, =CH), 50.6 (d, NCH), 23.9 (q, CH_3). HRMS calcd. for C14H10N2: 216.1626; found 216.1617.

Thermolysis of 1,6-diisopropyl-1,6-diazacyclodeca-3,8-diyne (1b) in presence of catalytic amounts of palladium at 85 - 120 °C. The same amounts, solvents and reaction apparatus was used as in the experiment at 140 °C. The reaction times and temperatures are given in Table 1. After removal of the solvent the product was analyzed without further purification by NMR and GC/MS to yield N,N'-diisopropyl-3,3'-bispyrrole (**2b**), N,N'-diisopropyl-2',5'-dihydro-3,3'-bispyrrole (**3b**) and N,N'-diisopropyl-4,5-2',5'-tetrahydro-3,3'-bispyrrole (**4b**) in the yields given in Table 1. Compound **3b** was purified by column chromatography on silica gel ($CHCl_3/CH_2OH$, 10:1). **3b**: 1H NMR δ: 6.66 (m, 2 H, =C-H (arom)), 6.22 (m, 1 H, =CH (arom)), 5.71 (m, 1 H, =C-H), 4.18 (hept., ^3J = 6.6 Hz, 1 H), 3.75 (m, 2 H, CH_2N), 3.63 (m, 2 H, CH_2N), 2.73 (hept., ^3J = 6.3 Hz, 1 H), 1.43 (d, ^3J = 6.6 Hz, 6 H), 1.15 (d, ^3J = 6.3 Hz). ^{13}C NMR δ: 134.6 (s, =C-), 119.1, 118.6 (2 x d, =CH), 115.8 (s, =C-), 115.7, 105.7 (2 x d, =CH), 58.4, 58.0 (2 x t, CH_2N), 54.5, 50.9 (2 x d, NCH), 23.9, 23.8, 21.4 (3 x q, CH_3). HRMS calcd. for $C_{14}H_{22}N_2$: 218.1783; found 218.1766. **4b**. ^1H NMR δ: 5.57, 5.52 (2 x m, 2 H, =CH), 3.71, 3.59, 3.20, 3.13 (4 x m, 8 H, CH_2), 2.6 - 2.7 (2 x hept., 2H, NCH), 1.11 -1.10 (d, 12 H, CH_3). ^{13}C NMR δ: 135.2, 131.5 (2 x s, =C-), 123.2, 120.2 (2 x d, =CH), 58.1, 57.4 (2 x t, CH_2), 54.2, 53.7 (2 x d, NCH), 51.2, 48.3 (2 x t, CH_2), 21.7, 21.4 (2 x q, CH_3). HRMS calcd. for $C_{14}H_{24}N_2$: 220.193; found 220.1884.

Catalytic reduction of N,N'-diisopropyl-2',5'dihydro-3,3'-bispyrrole (3b). A solution of 60 mg (0.3 mmol) of **3b** in 60 ml methanol and 10 mg (0.003 mmol) palladium (80% Pd/C) was heated at 80 °C and hydrogen atmosphere (60 bar) for 16 h. After removal of the solvent the residue was purified by chromatography on Al_2O_3 III (cyclohexane / ethyl acetate 1:1) to yield 22 mg (33%) of N,N'-diisopropyl-2',3',4',5'-tetrahydro-3,3'-bispyrrole (**12b**) as a colorless, waxy solid which turned into a brown color when exposed to air. **12b**: ^{1}H NMR δ: 6.64, 6.54, 6.01 (3 x m, 3 H, =CH), 4.16 (hept., 1 H, NCH), 3.28 (m, 1 H, NCH_2), 3.24 (m, 1 H, CH), 3.01 (m, 1 H, NCH_2), 2.52 (m, 1 H, NCH), 2.43 (hept., 1 H, NCH), 2.32 (m, 1 H, NCH_2), 2.23 (m, 1 H, CH_2), 1.80 (m, 1 H CH_2), 1.42 (d, 6 H, CH_3), 1.12 (2 x d, 6 H, CH_3). ^{13}C NMR δ: 126.2 (s, =C-), 118.2, 115.0 (2 x d, CHN), 106.2 (d, =CH), 59.9 (t, NCH_2), 55.2 (d, NCH),51.8 (t, NCH_2), 50.6 (d, NCH), 36.1 (d, CH), 32.7 (t, CH_2), 23.9 (2 x q, 2 x CH_3), 21.5, 21.4 (2 x q, 2 x CH_3). HRMS calcd. for $C_{14}H_{24}N_2$: 220.1943; found 220.1941.

Thermolysis of 1,6-diazacyclodeca-3,8-diyne (1a) in presence of catalytic amounts of palladium at 140 °C. A solution of 268 mg (2 mmol) of 1,6-diazacyclodeca-3,8-diyne (**1a**) in 110 ml of methanol was heated under stirring with 10 mg (0.003 mmol) of palladium (10%, Pd/C) at 140 °C for 2 h in an autoclave. The work-up was carried out as for **1b**, it yielded 135 mg (50%) of 3,3'bipyrrole (**2a**). The reported data of **2a**[9] were identical with that of the product. **2a**: ^{1}H NMR (300 MHz, $CDCl_3$) AA'BB'CC'X_2 system, δ: 8.10 (s, 2H, NH), 6.91 (m, 2H, =CHN), 6.78 (m, 2H, =CHN), 6.39 (m, 2H; =CH). ^{13}C NMR δ; 119.7 (s, =C-), 118.2, 113.3, 106.8 (3 x d, =CH). **2c:** ^{1}H NMR (300 MHz), δ: 7.45 - 7.39, 7.24 - 7.20, 7.11 - 7.09, 6.53 - 6.51 (4 x m, C_{Ar}-H). ^{13}C NMR (75.46 MHz), δ: 129.5 (d, C_{Ar}-H), 129.0 (s, Ph-C=), 125.3 (d, C_{Ar}-H),126.1 (s, pyrrole =C-), 120.1 (d, C_{Ar}-H), 119.7 (d, pyrrole =C-), 114.7 (d, pyrrole =C-), 109.0 (d, pyrrole =C-).

Thermolysis of 1,6-diphenyl-1,6-diazacyclodeca-3,8-diyne (1c) in presence of catalytic amounts of palladium. A solution of 286 mg (1 mmol) of 1,6-diphenyl-1,6-diazacyclodeca-3,8-diyne (1c) in 110 ml of methanol was heated under stirring with 10 mg (0.003 mmol) of palladium (10% Pd/C) at 140 °C for 2 h in an autoclave. The work-up was carried out as for **1b**. The crude product was purified by column chromatography on silica gel (cyclohexane / toluene 3:1) to yield 151 mg (53%) of N,N'diphenyl-3,3'bipyrrole (**2c**) as colorless air sensitive crystals. **2c**: ^{1}H NMR δ: 7.45 - 7.39, 7.24 - 7.20, 7.11 - 7.09, 6.53 - 6.51 (4 x m, C_{Ar}-H). ^{13}C NMR δ: 129.5 (d, C_{Ar}-H), 129.0 (s, Ph-C=), 125.3 (d, C_{Ar}-H),126.1 (s, pyrrole =C-), 120.1 (d, C_{Ar}-H), 119.7 (d, pyrrole =C-), 114.7 (d, pyrrole =C-), 109.0 (d, pyrrole =C-). HRMS calcd. for $C_{20}H_{16}N_2$: 284.1333; found 284.1323.

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