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A Palladium Catalyzed Domino Coupling Process to Substituted Phenanthrenes

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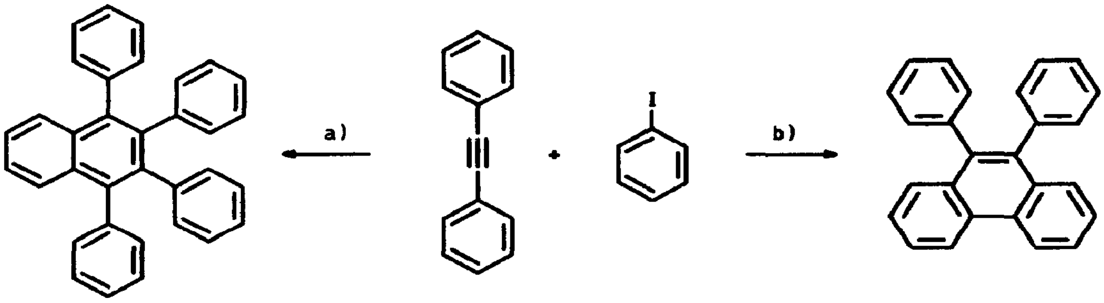
Abstract: A palladium catalyzed annulation reaction of diphenylacetylene with iodobenzene leads to 9,10-diphenylphenanthrene. The regiochemistry of this domino coupling process is studied, suggesting the cis-trans isomerization of vinyl palladium complexes as reactive intermediates.

Domino coupling processes are a fascinating topic of current research, since they enable the synthesis of complex target molecules from simple starting materials in a single preparative step.[1] The formation of the substituted naphthalene **1** as a 2:1-product from diphenylacetylene **2** and iodobenzene **3** under palladium catalysis represents an example of such a sequential transformation.[2] Recently we reported that in this case a minor change in reaction conditions strongly influences product formation.[3] Thus, replacing triphenylphosphine/nitromethane as the ligand/solvent system by the coordinating solvent dimethylformamide (DMF) leads to the formation of the substituted phenanthrene **4** as a 1:2-product in good yield. Most interestingly **4** is still by far the main product when the starting materials **2** and **3** are used as a 2:1 mixture.

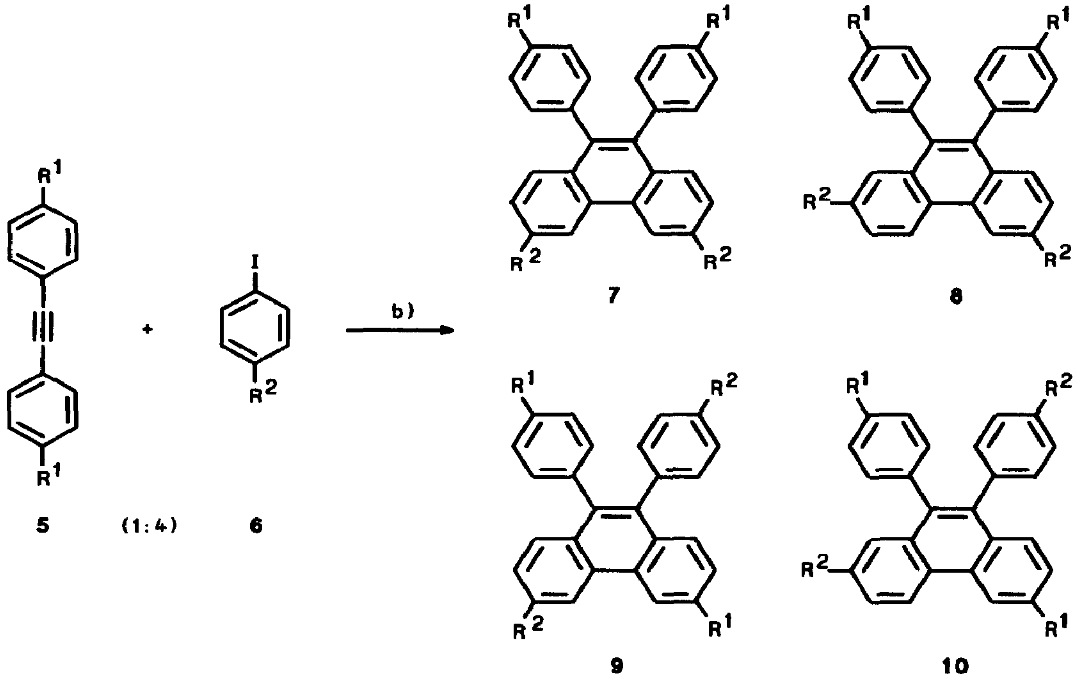


1 **2** **3** **4**

0.5 equiv. **3**: 47 %

a) 2 Mol-% $Pd(OAc)_2$, PPh_3, Et_3N, $MeNO_2$, 100 °C, 3 d;
b) 5 Mol-% $Pd(OAc)_2$, K_2CO_3, $n\text{-}Bu_4NBr$, DMF, 100 °C, 3 d.

10 equiv. **3**: 88 %
4 equiv. **3**: 77 %
2 equiv. **3**: 69 %
0.5 equiv. **3**: 58 %



entry	R^1	R^2	total yield [c] [%]	product ratio [%] [d]			
				7	**8**	**9**	**10**
1	OMe	OMe	38	62*	38*	-	-
2	OMe	H	89	60*	-	40*	-
3	OMe	CO_2Me	60	36*	43*	11	10
4	H	OMe	57	20*	35*	7	38*
5	H	H	77	100*	-	-	-
6	H	CO_2Me	60	31*	50*	4*	15*
7	CO_2Me	OMe	47	22	67*	11 [e]	
8	CO_2Me	H	52	93*	-	7*	-
9	CO_2Me	CO_2Me	25	88*	12	-	-

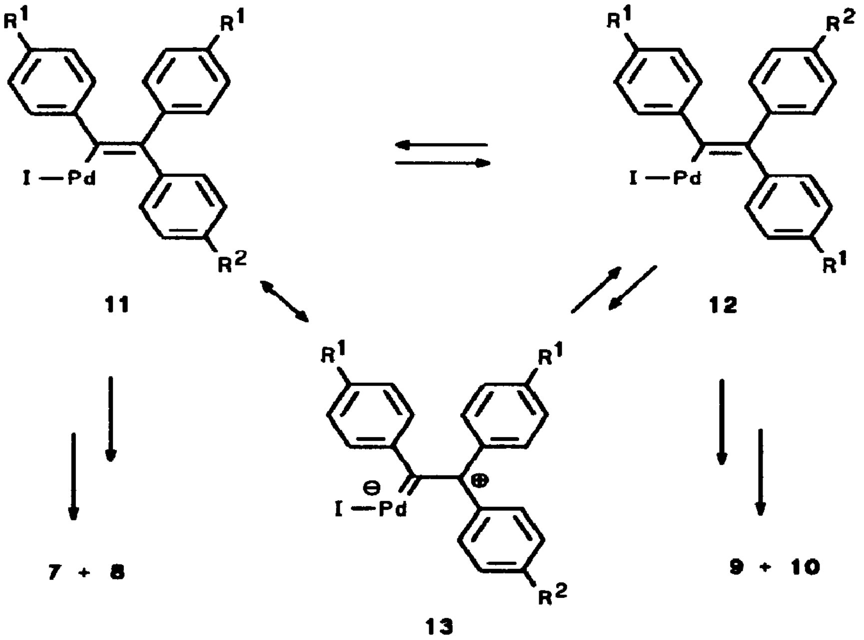
b) 5 Mol-% $Pd(OAc)_2$, K_2CO_3, $n\text{-}Bu_4NBr$, DMF, 100 °C, 3 d; c) total yield of isolated 9,10-diphenylphenanthrenes is given; d) determined by ^1H NMR analysis of the crude product; e) **9.7** and **10.7** combined; *: these products were isolated by flash chromatography or MPLC and fully characterized by spectroscopic means (^1H NMR, ^{13}C NMR, IR, UV, MS and elemental analysis).[4]

In order to clarify the regiochemistry of this domino coupling process the reactions of para-substituted derivatives **5** and **6** of diphenylacetylene **2** and iodobenzene **3** have been studied. Moreover the systematic permutation of methoxy, carboxylic ester and hydrogen substituents should eventually reveal electronic effects.

As a result up to four regioisomeric 1:2-products (**7**, **8**, **9** and **10**) can be identified. For reasons of symmetry this reaction scheme is simplified in certain cases: with $R^1 = R^2$ for instance **7** and **9** as well as **8** and **10** are identical (entries 1 and 9), with $R^2 = H$ on the other hand **7** and **8** as well as **9** and **10** are identical (entries 2 and 8).

The observed domino coupling process obviously is closely related to palladium catalyzed annulation reactions of aryl halides with norbornene that have been thoroughly investigated with regard to the mechanism.[5] Accordingly, the vinyl palladium complex **11**[6] is presumably formed by a syn-addition[7] of an aryl palladium halide to the acetylenic triple bond. Since cyclometallation of **11** should ultimately lead to the products **7** and **8** (in analogy to the similar annulation reactions at norbornene[5]) the formation of the therefore unexpected products **9** and **10** should proceed via the stereoisomeric vinyl palladium complex **12**. Appreciable amounts of **9** and **10** obviously are detected when electron donating methoxy substituents are present (entries 2 and 4)[8]. In these cases the cis-trans isomerization of the vinyl palladium complexes **11** and **12** might be feasible due to the weakness of the alkene bond as illustrated by the dipolar resonance structure **13**.

In contrast, the ester function in para position as an electron acceptor seems to inhibit the formation of **9** and **10** (entry 7 and 8)[8]. Therefore radical intermediates that would be even



better stabilized by electron acceptors than by the electron donating anisyl group[9] can be ruled out for the cis-trans isomerization.

From a preparative point of view satisfying overall yields of phenanthrene derivatives are usually obtained. Entry 9 is an exception: in this case the relatively electron-poor acetylene **5** only sluggishly reacts and the Ullmann coupling[10] of **6** (R = CO_2Me) to give the corresponding biphenyl-4,4'-dicarboxylic acid ester becomes the main reaction pathway.

In summary, the domino coupling process of diarylacetylenes with aryl halides represents a valuable new approach to substituted phenanthrenes. The extension of this method towards the synthesis of polycyclic hetarenes is currently under investigation.

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4. Melting points (uncorrected) and selected ^{1}H NMR data (400.1 MHz, $CDCl_3$, TMS) of the diagnostic region between δ = 8.00 and 10.0 ppm: **7.1** (mp 255 ^{o}C): 8.05 (2 Hz); **8.1** (mp 252 ^{o}C): 8.60 (9 Hz), 8.04 (2 Hz); **7.2** (mp 246 ^{o}C): 8.79 (8 Hz); **9.2** (mp 251 ^{o}C): 8.71 (8 Hz), 8.16 (2 Hz); **7.3** (mp 252 ^{o}C): 9.60 (2 Hz), 8.10 (9 Hz, 2 Hz); **8.3** (mp 241 ^{o}C): 9.52 (2 Hz), 8.92 (9 Hz), 8.33 (2 Hz), 8.29 (9 Hz), 8.10 (9 Hz), **9.3**: 9.43 (2 Hz); **10.3**: 8.90 (9 Hz); **7.4** (mp 178 ^{o}C): 8.08 (2 Hz); **8.4** (mp 182 ^{o}C): 8.62 (9 Hz), 8.06 (2 Hz); **9.4** = **9.2**; **10.4** (mp 241 ^{o}C): 8.69 (9 Hz), 8.68 (8 Hz); **7.5** (mp 239 ^{o}C): 8.80 (8 Hz); **7.6** (mp 258 ^{o}C): 9.61 (2 Hz), 8.11 (9 Hz); **8.6** (mp 253 ^{o}C): 9.53 (2 Hz), 8.93 (9 Hz), 8.32 (2 Hz), 8.31 (9 Hz), 8.13 (9 Hz, 2 Hz); **9.6** (mp 276 ^{o}C): 9.54 (2 Hz), 8.92 (8 Hz), 8.07 (9 Hz); **10.6** (mp 248 ^{o}C): 8.85 (8 Hz), 8.84 (8 Hz), 8.29 (2 Hz), 8.28 (9 Hz); **7.7**: 8.06 (2 Hz); **8.7** (mp 277 ^{o}C): 8.63 (9 Hz), 8.06 (2 Hz); **9.7** and **10.7**: 9.43 (2 Hz); **7.8** (mp 305 ^{o}C): 8.82 (8 Hz); **9.8** = **9.6**; **7.9** (mp 322 ^{o}C): 9.62 (2 Hz), 8.13 (8 Hz, 2 Hz); **8.9**: 9.57 (2 Hz).
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