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Palladium-catalyzed reaction of a sterically constrained trialkyne: a dimerization-type reaction with a surprising finale

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Abstract

The intramolecular reaction of a triyne promoted by palladium results in the formation of an enyne and coupling of the third alkyne with the phosphine. © 2000 Elsevier Science Ltd. All rights reserved.

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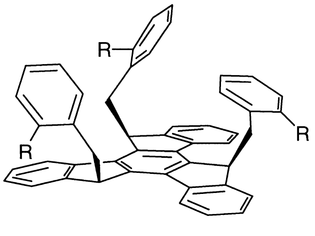
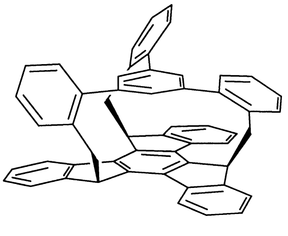
Among the variety of transition metals that are able to catalyze the [2+2+2] trimerization of alkynes,[1] cobalt-catalyzed processes have been the most widely applied in organic synthesis for the preparation of substituted benzenes.[2] We have recently described the synthesis of *syn*-truxene derivatives **1** by the Stille coupling reaction of **2** with trimethylsilylethynyltributylstannane, followed by desilylation.[3] Although cyclotrimerization of alkynes has been so far very rarely applied for the preparation of cyclophanes,[4] we decided to examine the prospect of using **1** as a starting material for the synthesis of cyclophane **3**[5] or related cyclophanes. Herein we report the synthesis of **3** by using a cobalt-mediated reaction and the formation of a new cyclophane by a reaction promoted by a palladium complex in which the phosphine ligand leads to an unexpected transmetalation reaction.



1 : R = C≡CH
2 : R = Br



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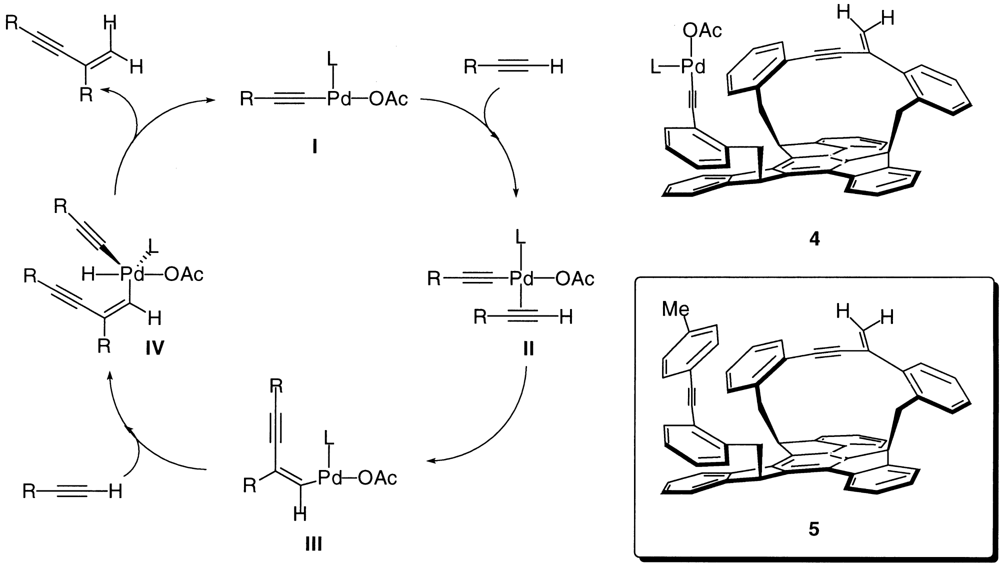
Recently, new pathways for the trimerization of alkynes have been uncovered by Yamamoto by using palladium catalysts.[6,7] However, simple terminal alkynes usually undergo dimerization in the presence of palladium catalysts to give either head-to-tail or head-to-head butenynes.[8–10] The mechanism suggested by Trost for the formation of heat-to-tail butenynes is summarized in Scheme 1.[9b] In this new proposal, three alkyne molecules are involved in the catalytic cycle. Importantly, the last alkyne was proposed to cleave the alkenylpalladium intermediate **III** by oxidative addition to form a Pd(IV) complex **IV**,[11] which evolves by reductive elimination to form the enyne and the catalytically active alkynylpalladium(II) complex **I** (Scheme 1). An alternative to this mechanism involved *trans*-dialkynyl palladium complexes as intermediates (σ-alkynyl instead of OAc for **I**–**IV**).

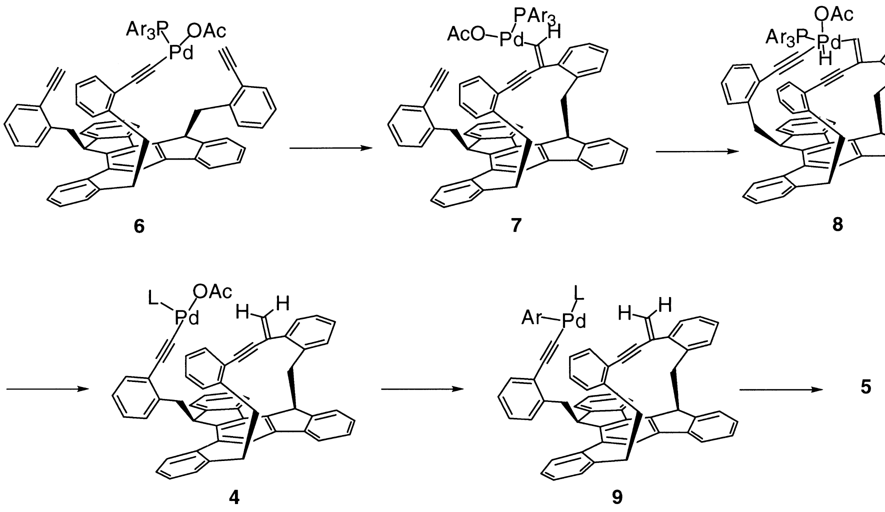


Scheme 1.

Truxene **1** appeared to be ideally suited to undergo the reactions outlined in Scheme 1 to give, after one turn of the cycle, palladium complex **4**. By using stoichiometric amounts of palladium, complex **4** was expected to be isolable due to the steric constraints introduced by the butenyne and truxene portions. On the other hand, formation of the butenyne was not expected if the process involved highly strained *trans*-dialkynyl palladium complexes as intermediates.

We therefore examined the reaction of triyne **1** by using different palladium complexes. The use of $Pd(PPh_3)_4$ or $Pd_2(dba)_3$·dba resulted in the formation of complex reaction mixtures. Interestingly, when trialkyne **1** was treated with stoichiometric $Pd(p\text{-}Tol_3P)_2(OAc)_2$, the new cyclic compound **5** was isolated in 30% yield.[12] The EI-MS of this new truxenephane revealed the presence of an additional *p*-tolyl group. The structure of this compound was assigned on the basis of its NMR spectra, including NOESY, HMBC and HMBQ experiments.[13] Particularly diagnostic were the NOEs observed between the methylene hydrogens of the enyne (broad singlet at 4.94 ppm) with two hydrogens of different benzyl groups (4.01 and 2.10 ppm).

The enyne of cyclophane **5** results from a head-to-tail coupling promoted by palladium.[8,9] Remarkably, a *p*-tolyl group from the triarylphosphine is attached to the third alkyne. Formation of **5** can be rationalized as shown in Scheme 2. Thus, insertion of the second alkyne into the alkynyl–palladium bond of **6** would give **7**. Presumably, and in accordance with Scheme 1, oxidative addition of the terminal C–H bond of the alkyne would give rise to complex **8**,[11] that could give **4** by reductive elimination (L = phosphine and/or enyne). The palladium of intermediate **4** could be either coordinating the enyne or a molecule of *p*-Tol_3P. Surprisingly, **4** undergoes a transmetalation-type reaction with *p*-Tol_3P to form **9**, which would give rise to the final organic product **5**.



Scheme 2.

Under forcing conditions, PPh_3 is known to react with $Pd(OAc)_2$ to form $[PhPd(PPh_3)(\mu\text{-}OAc)]_2$.[14] Thus, this palladium complex may initiate the series of reactions outlined in Scheme 2 (Ph instead of OAc). Alternatively, the penultimate step (**4**→**9**) could proceed by coupling of the terminal arylacetylene with a phosphonium salt formed by the reductive elimination of an alkynyl (i.e. **6** or **4**) or alkenyl (i.e. **7**) palladium intermediate.[15,16] Indeed, this type of cross-coupling was also observed in the reaction between phenylacetylene with *p*-Tol_3P (2 mol equiv) in the presence of $Pd(OAc)_2$ (1 mol equiv.) (70°C, 20 h), which affords *p*-tolylphenylacetylene, although in low yield.[17] Thus, the macrocycle prevents further coupling of alkynyl–Pd complex **4** and favors the arylation reaction.

While benzannulation of the alkynes of **1** could not be achieved by using palladium catalysts, heating **1** in xylene with a stoichiometric amount of $CpCo(CO)_2$ lead to cyclophane **3** in 15% yield.

In summary, while cobalt-mediated benzannulation of trialkyne **1** affords cyclophane **3**, palladium-promoted reaction of **1** leads to a head-to-tail enyne **5**. Interestingly, an aryl group from the triarylphosphine ligand is incorporated into the third alkyne. Formation of the new cyclophane **5** in the presence of palladium is in accordance with the catalytic cycle shown in Scheme 1 for the synthesis of butenynes in the palladium-catalyzed dimerization of terminal alkynes.

Acknowledgements

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11. Alternatively, the acidic C–H bond of the alkyne could cleave the alkenyl–Pd bond of **III** to give the butenyne and the alkynyl–Pd complex **1**.
12. A similar compound was obtained with $Pd(PPh_3)_2(OAc)_2$. However, assignment of the ^1H NMR of this truxenephane was complicated due to superposition of several of the Ar–H resonances.
13. ***Experimental***. A solution of palladium acetate (28 mg, 0.12 mmol) and tri(*p*-tolyl)phosphine (75 mg, 0.25 mmol) in toluene (50 ml) was warmed to 60°C and treated dropwise with a solution of **1** (50 mg, 0.073 mmol) in toluene (8 ml). The resulting black mixture was heated at 70°C for 4.5 h. After being cooled to room temperature, the mixture was evaporated and the residue was chromatographed (100:1:1 to 100:2:1 hexane:EtOAc:CH_2Cl_2) to give **5** (17 mg, 23%): ^1H NMR ($CDCl_3$, 300 MHz, 15 mM) δ 7.99 (d, $J=7.7$ Hz, 1H), 7.98 (d, $J=7.7$ Hz, 1H), 7.96 (d, $J=7.7$ Hz, 1H), 7.75 (d, $J=7.7$ Hz, 1H), 7.51 (dd, $J=2.0$, 6.9 Hz, 1H), 7.43 (d, $J=7.3$ Hz, 1H), 7.12–7.41 (m, 10H), 7.08 (br d, $J=7.7$ Hz, 1H), 7.01 (t, $J=7.7$ Hz, 1H), 6.97 (t, $J=7.7$ Hz, 1H), 6.88 (d, $J=8.1$ Hz, 2H), 6.50–6.61 (m, 3H), 6.48 (d, $J=7.3$ Hz, 1H), 6.18 (d, $J=6.9$ Hz, 1H), 4.97 (t, $J=3.6$ Hz, 1H), 4.94 (s, 2H), 4.64–4.75 (m, 2H), 4.12 (dd, $J=3.6$, 12.5 Hz, 1H), 4.01 (dd, $J=9.6$, 14.1 Hz, 1H), 3.64 (dd, $J=8.1$, 13.7 Hz, 1H), 3.52 (dd, $J=4.8$, 13.7 Hz, 1H), 3.41 (dd, $J=4.0$, 12.5 Hz, 1H), 2.10 (dd, $J=10.9$, 14.1 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.21, 147.17, 143.28, 142.44, 141.60, 141.18, 140.84, 139.49, 138.62, 138.24, 137.96, 136.07, 135.73, 132.54, 132.23, 131.71, 130.69, 130.21, 129.37, 129.12, 128.68, 128.50, 128.03, 127.69, 127.46, 127.39, 127.00, 126.75, 126.62, 126.34, 126.24, 126.09, 125.97, 125.47, 123.61, 122.83, 122.18, 121.88, 120.40, 91.61, 91.37, 91.20, 88.26, 48.65, 47.82, 47.68, 37.42, 36.83, 35.52, 21.63; FAB-MS *m*/*z* 775 (71, M^++1), 774 (M^+, 72), 569 (61), 339 (100); FAB-HRMS calcd for $C_{61}H_{42}$ 774.3286; found 774.3249.
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17. It is interesting to note that the major new product was *p,p′*-dimethylbiphenyl. Heating *p*-Tol_3P with Pd(OAc)_2 in toluene (70°C, 20 h) in the absence of phenylacetylene leads also to the formation of *this* biphenyl as the major new product (isolated in 3% yield).