Domino Reactions

DOI: 10.1002/anie.201307793

A Domino Approach to Dibenzopentafulvalenes by Quadruple Carbopalladation**

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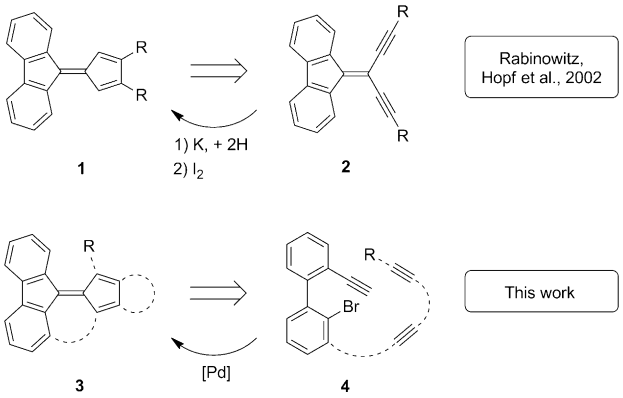
In memory of Michael Bendikov

Owing to their special electronic properties cross-conjugated systems have experienced a renaissance in recent years,[1] and also pentafulvalene and its substituted analogues have come back into focus.[2,3] Originally regarded as laboratory curiosities displaying nonplanar structures and unusual bond lengths and angles,[4] they have attracted attention as ligands[5] for transition metals and as two-electron acceptors affording aromatic dianions.[6] Whereas the parent fulvalene is unstable at temperatures above −78 °C,[7] the perchloro derivative shows completely reversible redox behavior.[6b] Further investigations with fulvalene vinylogues[6b] indicate properties conducive to tuning the performance of organic-based batteries on a molecular level.

The preparation of symmetrical pentafulvalenes has been realized for the most part by the coupling of two cyclopentadienyl rings, involving strong lithium bases and often molecular oxygen as the oxidant or $CuCl_2$ as the coupling promoter.[7,8] Other couplings have been performed by the Grignard addition to ketones[9] and homo couplings employing halogenated species and transition metals.[10] Also diazo compounds, which readily release nitrogen, have served as starting materials.[11] An alternative synthetic pathway investigated in the last decade accesses dibenzopentafulvalenes **1** by reductive Bergman-type cyclizations of cross-conjugated enediynes **2** (Scheme 1, top).[12]

Highly substituted unsaturated oligocyclic systems can also be prepared by carbopalladation reactions. In the last two decades a number of domino carbopalladation sequences have been developed, yielding homo- and heterocyclic systems such as lactones, chromanes, molecular switches,



Scheme 1. Retrosynthetic (synthetic) approaches to dibenzopentafulvalenes.

and further complex systems in one single step from relatively simple starting materials.[13–15]

Herein we disclose a novel dibenzopentafulvalene synthesis which affords the pentafulvalene framework in only one step through a quadruple carbopalladation process. Our retrosynthetic strategy relied on a readily available biphenylacetylene and two tethered alkyne moieties **4** (Scheme 1, bottom). We envisioned that a sequence starting with the oxidative addition of Pd into the C–Br bond followed by three carbopalladation steps to the C–C triple bonds and finishing with a final carbopalladation to the newly formed alkene would provide the dibenzopentafulvalene skeleton **3**.

To test our approach, we chose the biphenyl derivative **7** which was coupled with various diynes (Scheme 2). Biphenyl **7** was synthesized in two steps by the Suzuki–Miyaura coupling of the trisubstituted arene **5** and boronic acid **6** followed by removal of the silyl protecting groups in 75% overall yield. Various diynes were obtained by Sonogashira cross-coupling of terminal diyne **8**; the respective alcohols were transformed by Appel reaction into propargylic iodides **9**. Final nucleophilic substitution of **9** by the phenolic hydroxy group in **7** afforded the domino substrates **4** in good to excellent yields.

We initially chose substrate **4a** to optimize the reaction conditions. Table 1 compiles the effects of catalyst, additional ligand, solvent, temperature, and reaction time on the outcome of the domino process. In early stages of the screening triethylamine appeared to be the optimal base. The combination of toluene as the solvent and $[Pd(PPh_3)_4]$ as the catalyst was found to have the highest potential (Table 1, entries 1–5).

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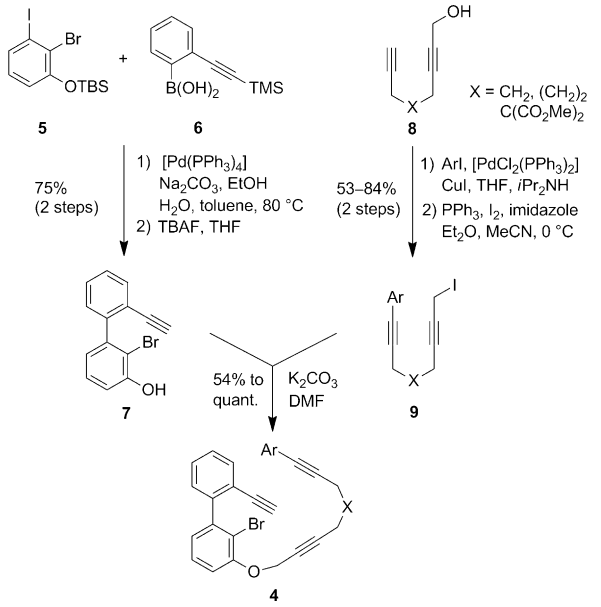
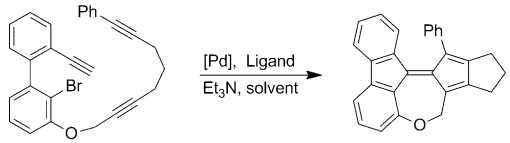
[**] We thank the German Research Foundation (DFG), the Danish National Research Foundation (DNRF), and the Fonds der Chemischen Industrie (Emmy Noether Fellowship, Heisenberg Fellowship, and Dozentenstipendium to D.B.W.). Furthermore, we are grateful to Sonja Schmidt for preparative assistance, and Dr. Markus Finger and Prof. Dr. Sven Schneider (University of Göttingen) for their help with the CV measurements.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201307793.



Scheme 2. Synthesis of the domino precursors.

Table 1: Optimization of the quadruple carbopalladation.[a]

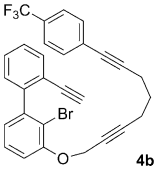
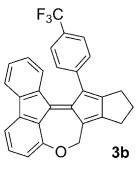
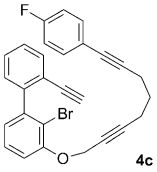
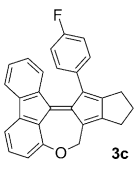
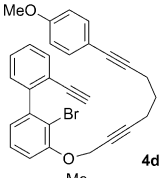
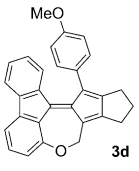
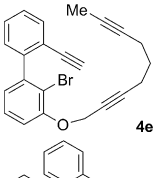
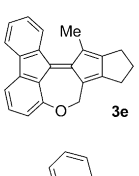
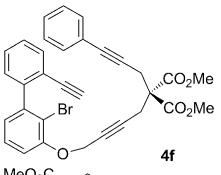
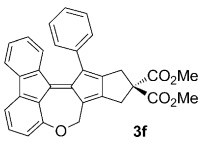
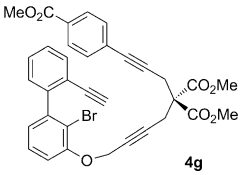
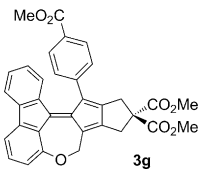
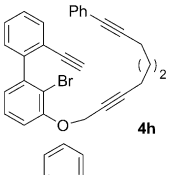
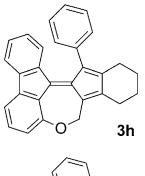
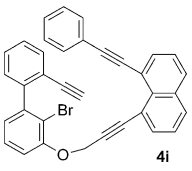
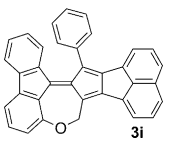


Entry	Catalyst	Ligand	Solvent	T [°C]	t [h]	Yield[b] [%]
1	$[Pd(PPh_3)_4]$	–	dioxane	100	20	traces
2	$Pd(OAc)_2$	–	toluene	100	20	15
3	$[Pd(PPh_3)_4]$	–	toluene	100	20	60
4	$[Pd(PPh_3)_4]$	–	DMF	100	20	traces
5	$[Pd(PPh_3)_4]$	–	MeCN	100	20	traces
6	$[Pd(PPh_3)_4]$	–	toluene	120	20	52
7	$[Pd(PPh_3)_4]$	–	toluene	60	20	71
8	$[Pd(PPh_3)_4]$	–	toluene	50	20	43
9	$Pd(OAc)_2$	PPh_3	toluene	60	20	59
10	$Pd(OAc)_2$	$P(o\text{-tol})_3$	toluene	60	20	47
11	$Pd(OAc)_2$	$P(C_6F_5)_3$	toluene	60	20	64
12	**$[Pd(PPh_3)_4]$**	**–**	**toluene**	**60**	**14**	**82**

[a] Reaction conditions: **4a** (1.0 equiv), catalyst (10 mol%), ligand (20 mol%), Et_3N (10 equiv), solvent (0.02 M). [b] Yield of isolated product based on **4a**.

Variation of the temperature was the key to further increase the yield. While a reaction temperature of 120 °C (entry 6) led to lower product formation, 60 °C (entry 7) appears to correspond to the optimal reactivity. A slightly lower reaction temperature of 50 °C (entry 8) resulted in a dramatic decrease in yield. Attempts to generate the active complex in situ and the usage of sterically more demanding or electron-deficient ligands (Table 1, entries 9–11) were associated with lower yields. Finally, we were able to achieve a yield of 82% by decreasing the reaction time from 20 to 14 h (Table 1, entry 12).[16]

Table 2: Scope of the quadruple domino carbopalladation.[a]

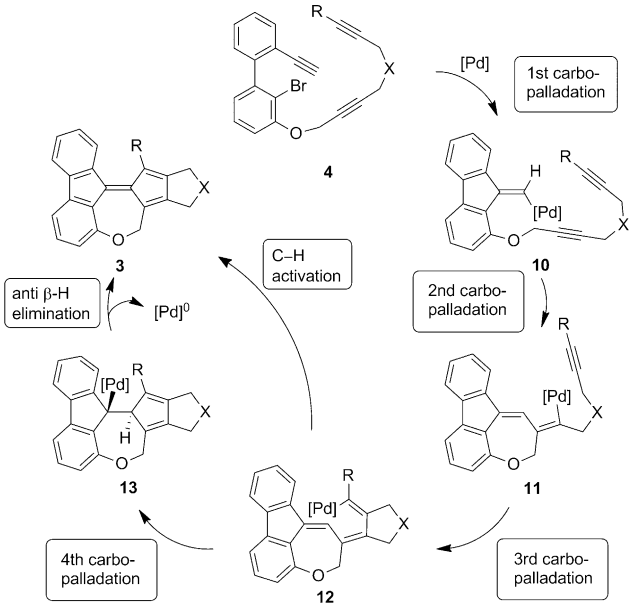
Entry	Substrate	Domino product	Yield[b] [%]
1			74
2			66
3			48
4			39
5[c]			84
6			55
7			53
8[d]			91

[a] Reaction conditions: **4** (1.0 equiv), catalyst (10 mol%), Et_3N (10 equiv), toluene (0.02 M), 14 h reaction time. [b] Yield of isolated product based on **4**. [c] 8 h reaction time. [d] 48 h reaction time.

To explore the scope of this transformation, we then applied the optimized reaction conditions to a range of substrates **4b–i** (Table 2). In all cases the respective dibenzopentafulvalenes **3b–i** were obtained. Electron-withdrawing and electron-donating substituents on the phenyl moiety were tolerated (Table 2, entries 1–3). A substrate with a terminal methyl residue instead of an aryl group proved to be less suitable (Table 2, entry 4); the significantly lower yield might be traced back to undesired β-H elimination at the methyl

group. The introduction of two ester groups in the tether reduced the reaction time to 8 h, probably as the result of the accelerating Thorpe–Ingold effect. When a naphthalene spacer (Table 2, entry 8) is incorporated in the substrate, the fully conjugated product **3i** was obtained in excellent yield; however, the reaction time had to be increased to 48 h because of the stiff substrate scaffold.

We suppose that the domino sequence is initiated by the oxidative addition of Pd^0 into the C–Br bond of biphenyl **4**. A first carbopalladation takes place with the ethynyl substituent of the biphenyl and leads to the fluorenyl framework **10** (Scheme 3). The next two carbopalladation steps employing



Scheme 3. Proposed mechanism to afford the dibenzofulvalenes.

the two triple bonds of the tether afford intermediate **12**. The final step might be regarded as a fourth carbopalladation of the newly formed central double bond terminated by β-H elimination. However, due to the *syn* attack of the Pd–C species, the hydrogen to be eliminated and the Pd are located on opposite sides of intermediate **13**. A typical β-H elimination taking place in a *syn* fashion cannot occur. Since the generated cyclopentadiene moiety shows increased acidity, the hydrogen might be lost as a proton. On the other hand, a negatively charged palladium species could be cleaved from **13** to furnish product **3**. Alternatively, one might regard the terminating step to be a C–H activation[17] of the triply substituted alkene by palladium which is in close proximity (Scheme 3).

Dibenzopentafulvalene derivative **3f** could be recrystallized to unambiguously prove the structure of the domino product by X-ray analysis (Figure 1).[18,19] The two cyclopentadienyl rings are slightly twisted relative to each other(dihedral angle 24.1°) to minimize steric interactions. The central double bond (1.371(2) Å) is longer than typical double bonds. The formal single bonds in the cyclopentadienyl rings

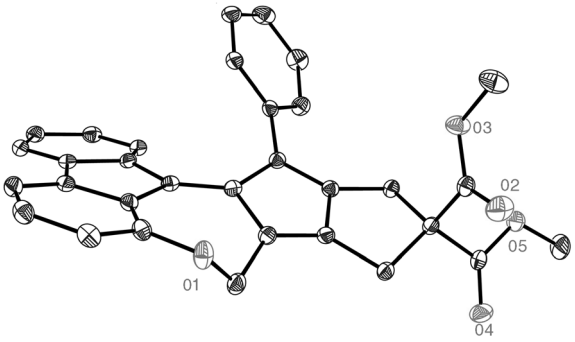


Figure 1. Molecular structure of dibenzopentafulvalene **3f** (H atoms are omitted for clarity). Thermal ellipsoids are given at the 50% probability level.[19]

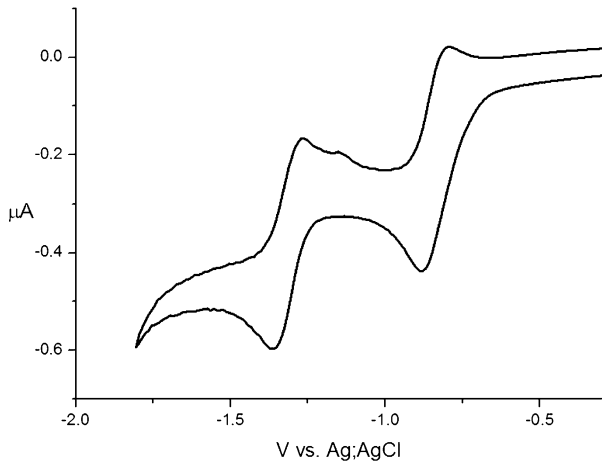


Figure 2. Cyclic voltammogram of dibenzopentafulvalene **3i** in MeCN (scan rate 250 $mV s^{-1}$).

range from 1.449(2) to 1.487(2) Å, indicating a high degree of delocalization.

The electrochemical properties of dibenzopentafulvalene **3i** were studied by cyclic voltammetry.[20] Two one-electron reduction steps were observed, the first at −0.88 V and the second at −1.36 V (Figure 2). Comparing this data to that of octachlorofulvalene, which exhibits strong electron-accepting properties,[6] the reduction potentials of **3i** are strongly shifted to higher absolute voltage demonstrating that reduction is more difficult. In line with this, oxidation of $\mathbf{3i}^{2-}$ is easier. If **3i** were to be used as an anodic unit in batteries, more energy could be gained than with the perchloro derivative. The difference between the first and second redox potentials of both systems is similar ($\Delta E = 0.48$ V) and indicates that the anionic and dianionic species of **3i** and octachlorofulvalene have comparable stability.

In summary, we have developed a novel synthetic route to highly substituted dibenzopentafulvalenes. The key step is a quadruple carbopalladation reaction building up the pentafulvalene framework. Nine different pentafulvalene systems were obtained in yields of 39–91%. The completely unsaturated system **3i** is able to take up two electrons in a reversible manner. Current efforts are directed toward

expanding the substrate scope as well as preparing other pentatria- or pentaheptafulvalenes by a similar methodology.

Received: September 4, 2013
Published online: November 7, 2013

Keywords: carbopalladation · domino reactions · fulvalenes · palladium

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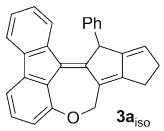

3a$_{iso}$

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[19] The crystal data and experimental details for the X-ray measurement are listed in the Supporting Information. CCDC 958071 (**3f**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[20] Not completely unsaturated dibenzopentafulvalenes did not show completely reversible redox behavior.