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Domino Reactions

A Fast Way to Fluorescence: A Fourfold Domino Reaction to Condensed Polycyclic Compounds

Lutz F. Tietze,*[a] Christoph Eichhorst,[a] Tim Hungerland,[a] and Markus Steinert[b]

Dedicated to Professor Alan Battersby on the occasion of his 90th birthday

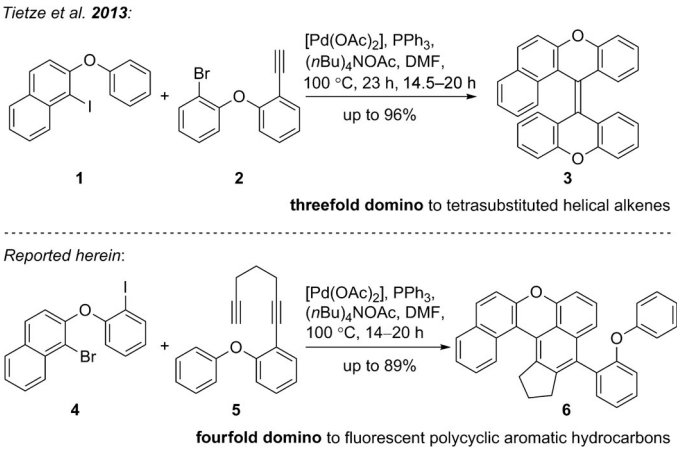
Abstract: A fast and efficient palladium-catalyzed fourfold domino Sonogashira/double-carbopalladation/C–H-activation reaction that converts simple aromatic systems into complex polycyclic hydrocarbons has been developed. A number of substituted products has thus been prepared in yields up to 89%. The structural assignment has been confirmed by using single-crystal X-ray crystallography. The products show intriguing fluorescence activity and thus might serve as chemical sensors or fluorescent imaging dyes.

Introduction

A quick and straightforward synthetic route that leads to either natural products or functional materials is the aim of every organic synthesis. To comply with these requirements, it is essential to develop facile reactions that easily transfer simple molecules into the desired complex structures in preferably few synthetic steps. Domino reactions fulfill these terms as they allow the incorporation of several reaction steps into one process without any intermediate purification.[1] Palladium-catalyzed domino reactions in particular have been in the focus of several recent publications.[2]

In a program aimed at the development and application of efficient palladium-catalyzed domino reactions, our group recently reported the synthesis of the natural products (+)- and (−)-linoxepin,[3a] (−)-diversonol,[3b] (−)-blennoide A,[3c] (−)-blennolide C,[3d] and (−)-gonytolide,[3d] as well as synthetic routes to tetrasubstituted helical alkenes as potential optical switches.[4] Thus, a threefold domino Sonogashira/carbopalladation/C–H-activation of **1** and **2** furnished alkene **3** in yields of up to 96% (Scheme 1).[4–7]

Herein we report the synthesis of condensed polycyclic compounds of type **6** by means of a fourfold two-component domino process using a diyne as one of the starting materials. The process includes a Sonogashira reaction, two carbopalladations, and one C–H-activation beginning with substrates **4** and **5**.



Scheme 1. Palladium-catalyzed domino reactions for the synthesis of functional materials.

Results and Discussion

The fourfold domino Sonogashira/double-carbopalladation/C–H activation reaction was optimized by employing iodide **4a** and dialkyne **5a** as substrates, and the best results were obtained using a 1:5 catalyst-to-ligand ratio that consisted of 1 mol% of $[Pd(OAc)_2]$ and 5 mol% of PPh_3 with tetrabutylammonium acetate as base (see Table 1).

The condensed pentacyclic compound **6a** was obtained in a yield of 73% (Table 1, entry 1). A reduction of the catalyst loading was not advantageous, since 0.5 mol% of $[Pd(OAc)_2]$ furnished only 58% of **6a** (Table 1, entry 2). Interestingly, increasing the catalyst loading of $[Pd(OAc)_2]$ from 1 to 5 and 10 mol% resulted in a decrease in the isolated yield from 73 to 66 and 62%, respectively (Table 1, entries 3 and 4). However, a catalyst/ligand ratio of 1:5 seems to be necessary. Neither

[a] Prof. Dr. L. F. Tietze, C. Eichhorst, Dr. T. Hungerland
Institut für Organische und Biomolekulare Chemie
Georg-August-Universität Göttingen
Tammannstrasse 2, 37077 Göttingen (Germany)
Fax: (+49) 551-39-9476
E-mail: ltietze@gwdg.de

[b] M. Steinert
Institut für Anorganische Chemie, Georg-August-Universität Göttingen
Tammannstrasse 4, 37077 Göttingen (Germany)

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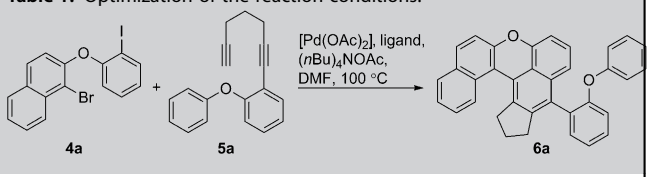
Table 1. Optimization of the reaction conditions.[a]



Entry	$[Pd(OAc)_2]$ [mol%]	Ligand	Ligand [mol%]	Yield [%][b]
1	1	PPh_3	5	73
2	0.5	PPh_3	2.5	58
3	5	PPh_3	25	66
4	10	PPh_3	50	62
5	1	PPh_3	2	66
6	1	–	–	28
7	10	$[P(tBu)_4][HBF_4]$	50	11
8	10	PCy_3	50	11
9	10	IPr·HCl	50	20
10	10	$P(4\text{-Cl-Ph})_3$	50	57
11[c]	10	PPh_3	50	45
12[d]	1	PPh_3	5	40

[a] Compound **4a** (1.1 equiv), **5a** (1.0 equiv), $[Pd(OAc)_2]$, ligand, $(nBu)_4NOAc$ (5 equiv), DMF, 100 °C, 14.5–21 h. [b] Isolated yields following flash column chromatography. [c] As in entry 1, but **4a** (1.0 equiv), **5a** (1.4 equiv), $(nBu)_4NOAc$ (6 equiv). [d] As in entry 1, but on a 1.1 mmol scale instead of 0.11 mmol.

a ratio of 1:2 (Table 1, entry 5) nor the use of $[Pd(OAc)_2]$ without any ligand (Table 1, entry 6) led to better results, as 66 and 28% yield were obtained, respectively. To further improve the reaction, the use of other ligands was also surveyed. Ionic ligand $[P(tBu)_4][HBF_4]$ led to **6a** in only 11% yield (Table 1, entry 7), which is equivalent to the result with the electron-rich PCy_3 ligand furnishing **6a** also in only 11% yield (Table 1, entry 8). An *N*-heterocyclic carbene (NHC) ligand was also used but gave a low yield of 20% (Table 1, entry 9). Electron-poor $P(4\text{-Cl—Ph})_3$, which is structurally similar to PPh_3, gave **6a** in an acceptable but slightly decreased yield of 57% (Table 1, entry 10). Thus, the results show that simple PPh_3 seems to be the best ligand for this transformation, which is consistent with previous investigations.[2e,5] Finally, experiments with different ratios of the two substrates, aryl iodide **4a** and dialkyne **5a**, revealed that the initially used 1.1:1 ratio gives the best results, considering that employing an inverse ratio of **4a** and **5a** of 1:1.4 delivered **6a** in only 45% yield (Table 1, entry 11). The optimized conditions used in entry 1 of Table 1 were also applied for a larger-scale synthesis of **6a**. However, the yields dropped, and only 40% of **6a** were isolated on a 1.1 mmol scale, compared to the 73% obtained on a 0.11 mmol scale (Table 1, entry 12).

Molecule **6a** was crystallized for structure elucidation through X-ray spectroscopy by dissolving **6a** in Et_2O and slowly evaporating the solvent in an *n*-hexane atmosphere. The crystallographic data show that in the single crystal of **6a** two molecules are included in a triclinic elementary cell (Figure 1).[8]

We then turned to investigating the scope of the reaction by introducing both electron-donating and electron-accepting groups in starting materials **4** and **5**. What's more, we also used substituted pyridines such as **4b** (Scheme 2). The fourfold

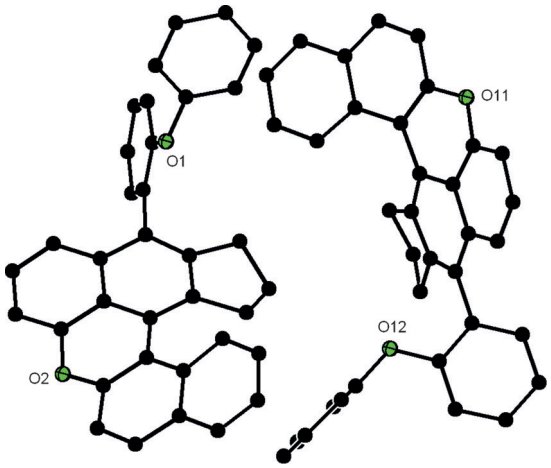
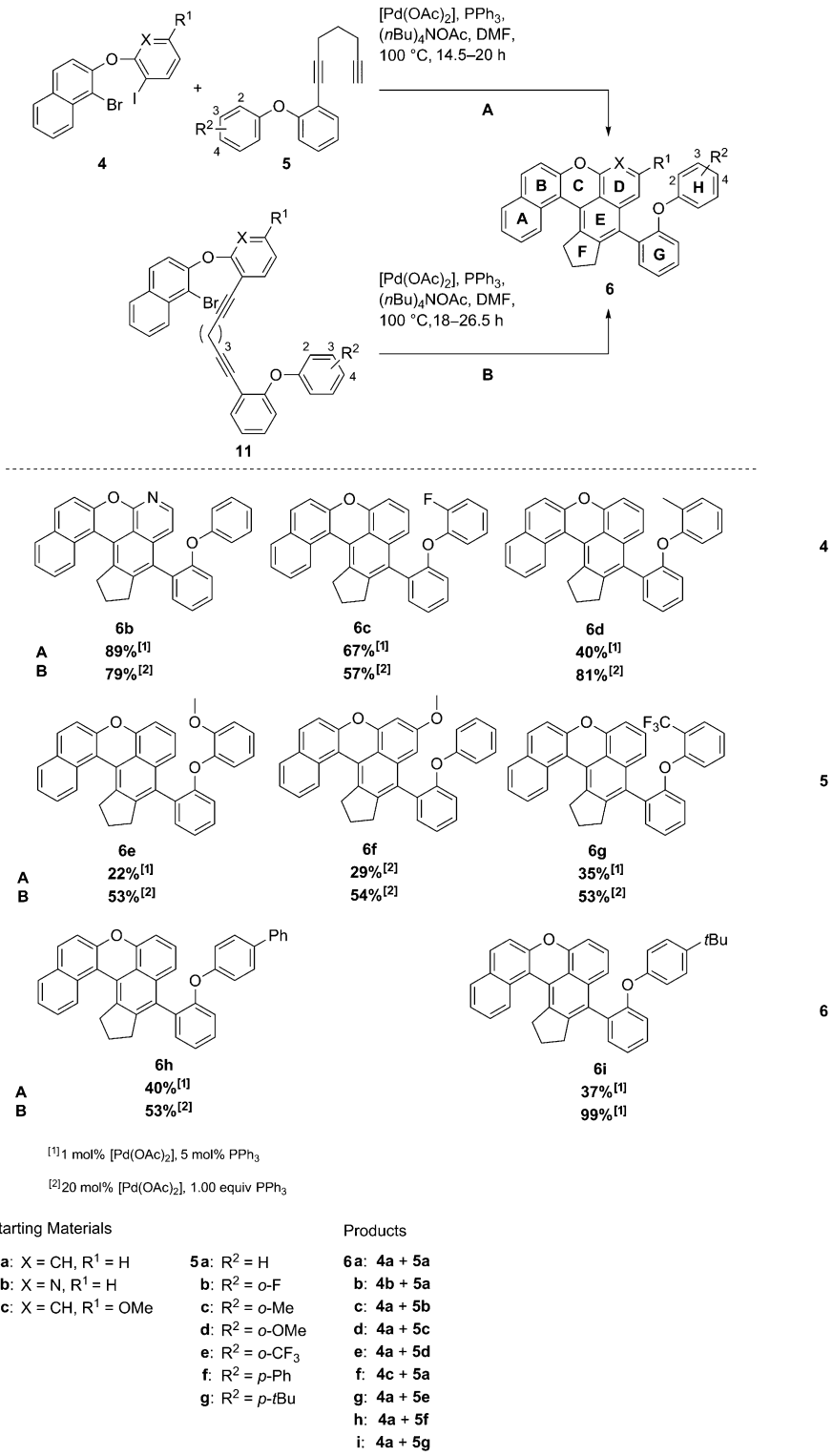


Figure 1. Molecular structure of **6a**. Hydrogen atoms have been omitted for clarity.

domino reaction of **4b** and **5a** gave 89% yield of **6b** when using 1 mol% of $[Pd(OAc)_2]$. Good results with 67% of **6c** were also obtained by reaction of **4a** and **5b**. The yields of the fourfold domino reactions of the other substrates to give **6d–i** were somewhat lower and reached 40 to 22% yield; we therefore slightly changed the protocol. We thus isolated the products of the initial Sonogashira reaction, which was then followed by a threefold domino double-carbopalladation/C—H-activation process. Consequently, the dialkyne substrates **5b–i** and **4a–c** were transformed into the Sonogashira products **7b–i** in 65 to 96% yield, which then led to **6b–i** through a Pd-catalyzed threefold domino reaction. Although the fourfold domino reaction gave better results than the threefold domino process for **6b** and **6c**, in all other cases the threefold domino process was superior. A striking example is the formation of **6i** when using 1 mol% $[Pd(OAc)_2]$, whereby the threefold domino process gave almost quantitative yield, whereas the fourfold reaction led to **6i** in only 37% yield under otherwise identical reaction conditions.

In general, the results show that a broad range of different substrates can be transformed to polycylic compounds **6** in good yields by using either the four- or threefold protocol. Even heterocycles can be incorporated, as shown with the preparation of substrate **6b**, which contains a pyridine ring.

The proposed mechanism of the fourfold and the corresponding threefold domino reactions of aryl halides **4** and dialkynes **5**, shown for **4a** and **5a**, begins with a Sonogashira reaction to give **7a** (Scheme 3). After an oxidative addition, a carbopalladation takes place to form **8a** containing a new C—C single bond and a vinyl–Pd species. The second carbopalladation again leads to the formation of a single bond and a vinyl–Pd species with concomitant formation of an aliphatic five-membered ring. At this point an *E*/*Z* isomerization from dialkene **9a** gives rise to the isomeric vinyl–Pd species **10a**, which can undergo formation of a single bond by means of a C—H-activation; in this transformation an acetate molecule might be involved. During the last step, both double bonds furnished in the domino process are incorporated into an aromatic system, thereby driving the reaction to completion.



Scheme 2. Products and corresponding yields for the fourfold and threefold domino reaction.

Owing to the rotation around the biphenyl axis in **6a** that connects the E to the G ring (compare with Scheme 2), the molecule showed dynamic effects in the NMR spectra. The structural lability led to temperature-dependent signal acuity in the ^{1}H NMR spectrum. Figure 2 shows the ^{1}H NMR spectrum of the aromatic region of **6a** at different temperatures. Whereas a temperature of 57 °C led to reasonably sharp coalescent signals, the signals are less well resolved at 25 °C. In contrast, at −37 °C the peaks of both isomers are resolved properly.

To determine the energy barrier of the isomerization process, 2D nuclear Overhauser effect spectroscopy (NOESY) experiments of **6a** were conducted at different mixing times (10^{-2} ms (reference time); 125, 250, 500, 1000 ms). The amplitudes of the diagonal and cross peaks at $\delta =$ 1.6 and 2.1 ppm were determined and the Exsycalc program by Mestrelab Research was used to calculate the corresponding reaction rate constants (k). By using the Eyring equation, the corresponding $\Delta G^{\neq}$ values were determined (Table 2). The measurements revealed an average value of $\Delta G^{\neq} = (69.7 \pm 2.3)$ kJ mol^{-1}.

Another interesting aspect is the fluorescence activity of the formed products **6**. Fluorescence markers are of interest for imaging experiments in biology and as chemical sensors.[11] Compound **6a** absorbs at a wavelength of 394 nm with an emission at 481 nm in acetonitrile (Figure 3).[12]

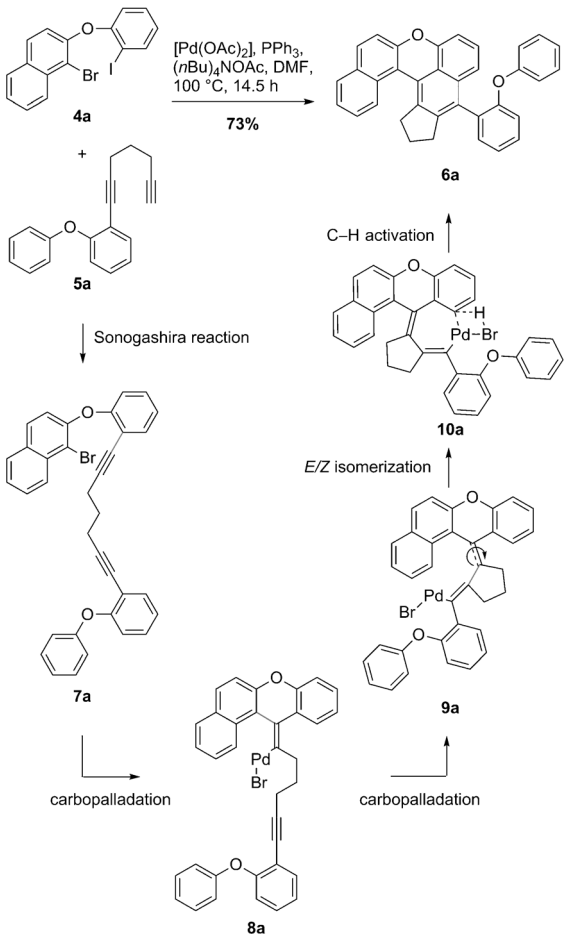
Conclusion

Highly productive and efficient fourfold and threefold domino reactions that consist of a Sonogashira reaction, two carbopalladations, and a C–H-activation process have been established that lead to condensed polycylic compounds that show strong fluorescence activity.

Experimental Section

Synthesis of 6a: General procedure for the fourfold domino reaction

A mixture of alkyne **5a** (29.1 mg, 112 μmol, 1.00 equiv), aryl iodide **4a** (50.0 mg, 118 μmol, 1.05 equiv), [Pd(OAc)$_2$] (251 μg, 1.12 μmol, 0.01 equiv), PPh$_3$ (1.47 mg, 5.60 μmol, 0.05 equiv), and (nBu)$_4$NOAc



Scheme 3. Proposed mechanism for the domino Sonogashira/double-carbopalladation/C–H-activation reaction of **4a** and **5a**. Ligands have been omitted for clarity.

(169 mg, 560 µmol, 5.00 equiv) in degassed DMF (3 mL) was stirred at 100 °C for 14.5 h. After cooling to RT, the solution was filtered through silica gel and the solvent of the filtrate was removed under vacuum. Column chromatography (silica gel, *n*-pentane/CH_2Cl_2 5:1) yielded the domino product **6a** (38.9 mg, 81.6 µmol, 73%) as a yellow solid. R_f = 0.48 (*n*-pentane/CH_2Cl_2 5:1); ^{1}H NMR (600 MHz, $C_2D_2Cl_4$, 100 °C, TMS): δ = 1.92 (br s, 2H), 2.73 (br s, 2H), 2.84 (dd, ^3J(H,H) = 6.7, 4.0 Hz, 2H), 6.79 (d, ^3J(H,H) = 7.7 Hz, 2H), 6.93 (t, ^3J(H,H) = 7.5 Hz, 1H), 6.96 (d, ^3J(H,H) = 7.6 Hz, 1H), 7.09–7.16 (m, 3H), 7.19 (d, ^3J(H,H) = 8.1 Hz, 1H), 7.25 (m_C, 1H), 7.31 (t, ^3J(H,H) = 7.5 Hz, 1H), 7.37 (dd, ^3J(H,H) = 8.8, 1.7 Hz, 1H), 7.40–7.49 (m, 3H), 7.52 (dd, ^3J(H,H) = 8.6, 6.7 Hz, 1H), 7.73 (d, ^3J(H,H) = 8.5 Hz, 1H), 7.82 (dd, ^3J(H,H) = 8.8, 1.5 Hz, 1H), 7.85 ppm (d, ^3J(H,H) = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $C_2D_2Cl_4$, 50 °C, TMS): δ = 26.5, 32.6, 36.5, 74.0, 106.7, 115.7, 116.8, 117.6, 118.5, 121.8, 122.7, 123.5, 124.2, 124.6, 125.1, 125.5, 125.5, 127.8, 128.1, 128.7, 129.1, 129.3, 129.7, 130.1, 130.8, 132.1, 133.0, 135.5, 145.7, 150.6, 153.3, 155.0 ppm; IR (ATR): $\tilde{\nu}$ = 1572, 1481, 1444, 1432, 1383, 1373, 1251, 1263, 1251, 1236, 1217, 810, 747, 735, 690 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (log ε) = 214 (4.8856), 266 (4.4164), 326 (3.9797), 353 (3.8447), 397 nm (3.9685); MS (ESI): *m/z* (%): 476.2 (100) $[M]^+$, 499.2 (76) $[M+Na]^+$; HRMS (ESI): *m/z* calcd for $C_{35}H_{24}O_2$: 476.1771; found: 476.1767 $[M+Na]^+$.

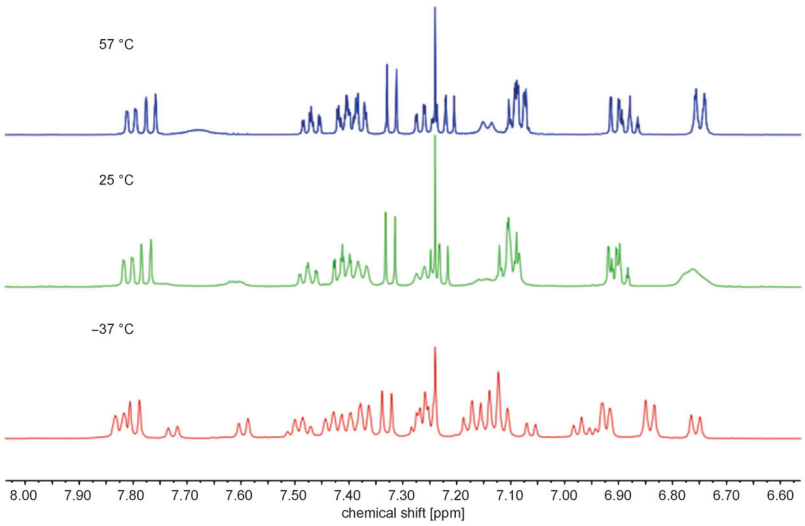


Figure 2. ^{1}H NMR spectrum of **6a** (aromatic region) at 57, 25, and −37 °C in $CDCl_3$.

Table 2. Calculation of $\Delta G^{\neq}$ of the rotation around the biphenyl axis in **6a** by means of Exsycalc at 295 K.

Entry	Mixing time [ms]	k [s^{-1}]	$\Delta G^{\neq}$ [kJ mol^{-1}]
1	1000	0.74	72.9
2	500	1.88	70.6
3	250	4.41	68.5
4	125	9.06	66.8

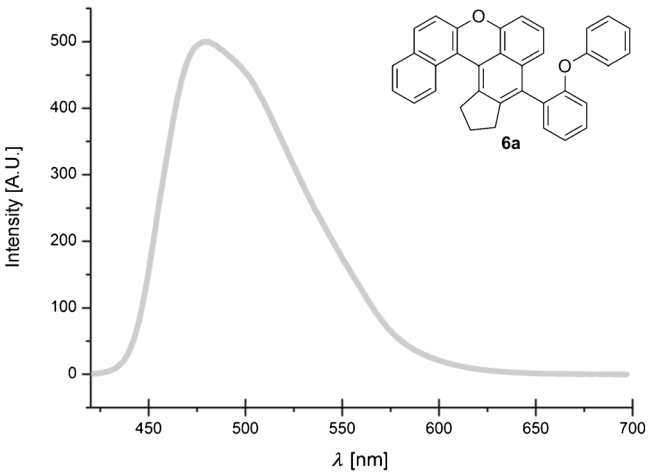


Figure 3. Fluorescence spectrum of **6a**.

Synthesis of 6i: General procedure for the threefold domino reaction

A mixture of **7i** (21.9 mg, 35.7 µmol, 1.00 equiv), $[Pd(OAc)_2]$ (80.1 µg, 3.57 µmol, 0.01 equiv), PPh_3 (468 µg, 17.9 µmol, 0.05 equiv), and $(nBu)_4NOAc$ (53.7 mg, 178 µmol, 3.00 equiv) in degassed DMF (3 mL) was stirred at 100 °C for 26.5 h. After cooling to RT, the reaction mixture was filtered through silica gel, flushed with EtOAc, and the solvent of the filtrate was removed under vacuum. Column chromatography (silica gel, *n*-

pentane/CH_2Cl_2 5:1) yielded the domino product **6i** (19 mg, 35.7 μmol, 99%) as a yellow solid. $R_f = 0.36$ (*n*-pentane/CH_2Cl_2 5:1); ^{1}H NMR (600 MHz, $C_2D_2Cl_4$, 100 °C, TMS): $\delta = 1.25$ (s, 9H), 1.94 (br s, 2H), 2.74 (br s, 2H), 2.84 (t, ^3J(H,H) = 6.8 Hz, 2H), 6.73 (d, ^3J(H,H) = 8.7 Hz, 1H), 6.96 (d, ^3J(H,H) = 7.5 Hz, 1H), 7.12 (d, ^3J(H,H) = 8.4 Hz, 1H), 7.15 (d, ^3J(H,H) = 8.7 Hz, 1H), 7.20 (d, ^3J(H,H) = 8.1 Hz, 1H), 7.26 (t, ^3J(H,H) = 8.0 Hz, 1H), 7.30 (t, ^3J(H,H) = 7.4 Hz, 1H), 7.38 (d, ^3J(H,H) = 8.7 Hz, 1H), 7.41–7.48 (m, 3H), 7.53 (t, ^3J(H,H) = 7.6 Hz, 1H), 7.77 (d, ^3J(H,H) = 8.4 Hz, 1H), 7.82 (d, ^3J(H,H) = 8.7 Hz, 1H), 7.86 ppm (d, ^3J(H,H) = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $C_2D_2Cl_4$, 50 °C, TMS): $\delta = 26.5$, 31.2, 32.6, 33.8, 36.6, 74.0, 106.7, 115.7, 116.9, 117.7, 118.3, 119.1, 121.8, 123.2, 124.2, 124.6, 125.0, 125.5, 125.5, 125.8, 127.8, 128.3, 128.7, 129.4, 129.7, 130.0, 130.8, 132.0, 133.0, 135.5, 145.7, 145.8, 150.6, 153.3, 154.5, 155.5 ppm; IR (ATR): $\tilde{\nu} =$ 3344, 3057, 2956, 2925, 2866, 1621, 1600, 1574, 1506, 1481, 1458, 1445, 1433, 1373, 1264, 1237, 1171, 1141, 1109, 1098, 1070, 1049, 1032, 1013, 1003, 982, 948, 923, 900, 877, 846, 832, 812, 784, 751, 736, 702, 665, 648, 637, 629, 606, 546 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log \varepsilon$) = 194 (5.2866), 213 (4.6149), 267 (4.1242), 326 (3.7003), 397 nm (3.6590); MS (ESI): *m/z* (%): 532.2 (100) $[M+H]^+$; HRMS (ESI): *m/z* calcd for $C_{39}H_{32}O_2$: 532.2397; found: 532.2402 $[M+H]^+$.

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Keywords: C–H-activation · domino reactions · dyes/pigments · luminescence · palladium

[1] a) *Domino Reactions: Concepts for Efficient Organic Synthesis*, Lutz F. Tietze (Ed), Wiley-VCH, Weinheim, **2014**; b) L. F. Tietze, S.-C. Düfert, J. Hierold, in *Domino Reactions: Concepts for Efficient Organic Synthesis* (Ed: L. F. Tietze), Wiley-VCH, Weinheim, **2014**, pp. 523–578; c) L. G. Voskressensky, A. A. Festa, A. V. Varlamov, *Tetrahedron* **2014**, *70*, 551–572; d) C. M. R. Chandra, I. Atodiresei, M. Rueping, *Chem. Rev.* **2014**, *114*, 2390–2431; e) H. Pellissier, *Chem. Rev.* **2013**, *113*, 442–524; f) J. Muzart, *Tetrahedron* **2013**, *69*, 6735–5785; g) L. F. Tietze, A. Düfert in *Modern Tools for the Synthesis of Complex Bioactive Molecules*, Wiley, Hoboken, NJ **2012**; h) H. Pellissier, *Adv. Synth. Catal.* **2012**, *354*, 5889–5891; i) L. F. Tietze, A. Düfert in *Catalytic Asymmetric Conjugate Reactions*, Wiley-VCH, Weinheim, **2010**, pp. 321–350; j) L. F. Tietze, G. Brasche, K. M. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim **2006**; k) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem.* **2006**, *118*, 7292–7344; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186; l) A. de Meijere, P. von Zezschwitz, S. Bräse, *Acc. Chem. Res.* **2005**, *38*, 413–422; m) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; n) L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*, 137–170; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131–163.

[2] a) M. Sickert, H. Weinstabl, B. Peters, X. Hou, M. Lautens, *Angew. Chem. Int. Ed.* **2014**, *53*, 5147–5151; b) E. E. Elboray, M. F. Aly, H. H. Abbas-Temirek, G. H. Churchill, R. Grigg, *Tetrahedron* **2014**, *70*, 110–122; c) C. Zheng, J. J. Chen, R. Fan, *Org. Lett.* **2014**, *16*, 816–819; d) S. R. Walker, M. L. Czyz, J. C. Morris, *Org. Lett.* **2014**, *16*, 708–711; e) L. F. Tietze, T. Hungerland, J. Ammermann, C. Eichhorst, S. O. Reichmann, D. Stalke, *J. Indian Chem. Soc.* **2013**, *90*, 1537–1555; f) Q. Liu, L. Wu, H. Jiao, X. Fang, R. Jackstell, M. Beller, *Angew. Chem.* **2013**, *125*, 8222–8226; *Angew. Chem. Int. Ed.* **2013**, *52*, 8064–8068; g) E. Kaneko, Y. Matsumoto, K. Kamikawa, *Chem. Eur. J.* **2013**, *19*, 11837–11841; h) R. Y. Nimje, M. V. Leskinen, P. M. Pihko, *Angew. Chem. Int. Ed.* **2013**, *52*, 4918–4922; i) R. Y. Nimje, M. V. Leskinen, P. M. Pihko, *Angew. Chem.* **2013**, *125*, 4918–4922; *Angew. Chem. Int. Ed.* **2013**, *52*, 4818–4822; j) J. Wallbaum, R. Neufeld, D. Stalke, D. B. Werz, *Angew. Chem.* **2013**, *125*, 13485–13488; *Angew. Chem. Int. Ed.* **2013**, *52*, 13243–13246; k) N. M. Groome, E. E. Elboray, M. W. Imman, H. Ali Dondas, R. M. Phillips, C. Kilner, R. Grigg, *Chem. Eur. J.* **2013**, *19*, 2180–2184; l) R. Grigg, S. Akkarasamiyo, N. Chuanopparat, E. Elboray, A. F. Moustafa, H. H. Abbas-Temirek, B. Kongkathip, N. Kongkathip, *Chem. Commun.* **2013**, *49*, 2007–2009; m) M. Leibeling, D. B. Werz, *Chem. Eur. J.* **2012**, *18*, 6138–6141; n) M. Leibeling, M. Pawliczek, D. Kratzert, D. Stalke, D. B. Werz, *Org. Lett.* **2012**, *14*, 346–349; o) X. Jia, D. A. Petrone, M. Lautens, *Angew. Chem.* **2012**, *124*, 10008–10010; *Angew. Chem. Int. Ed.* **2012**, *51*, 9870–9872.

[3] a) L. F. Tietze, S.-C. Duefert, J. Clerc, M. Bischoff, C. Maaß, D. Stalke, *Angew. Chem.* **2013**, *125*, 3273–3276; *Angew. Chem. Int. Ed.* **2013**, *52*, 3191–3194; b) L. F. Tietze, S. Jackenkroll, C. Raith, D. A. Spiegl, J. R. Reiner, M. C. Ochoa Campos, *Chem. Eur. J.* **2013**, *19*, 4876–4882; c) L. F. Tietze, L. Ma, J. R. Reiner, S. Jackenkroll, S. Heidemann, *Chem. Eur. J.* **2013**, *19*, 8610–8614; d) L. F. Tietze, S. Jackenkroll, J. Hierold, L. Ma, B. Waldecker, *Chem. Eur. J.* **2014**, *20*, 8628–8635.

[4] a) L. F. Tietze, T. Hungerland, M. A. Düfert, I. Objartel, D. Stalke, *Chem. Eur. J.* **2012**, *18*, 3286–3291; b) L. F. Tietze, T. Hungerland, C. Depken, C. Maaß, D. Stalke, *Synlett* **2012**, 2516–2520; c) L. F. Tietze, M. A. Düfert, T. Hungerland, K. Oum, T. Lenzer, *Chem. Eur. J.* **2011**, *17*, 8452–8461; d) L. F. Tietze, A. Düfert, F. Lotz, L. Sölter, K. Oum, T. Lenzer, T. Beck, R. Herbst-Irmer, *J. Am. Chem. Soc.* **2009**, *131*, 17879–17884.

[5] L. F. Tietze, T. Hungerland, C. Eichhorst, A. Düfert, C. Maaß, D. Stalke, *Angew. Chem.* **2013**, *125*, 3756–3759; *Angew. Chem. Int. Ed.* **2013**, *52*, 3668–3671.

[6] a) K. Gao, N. Yoshikai, *Acc. Chem. Res.* **2014**, *47*, 1208–1219; b) A. R. Kapdi, *Dalton Trans.* **2014**, *43*, 3021–3034; c) E. M. Ferreira, *Nat. Chem.* **2014**, *6*, 94–96; d) N. Yoshikai, Y. Wei, *Asian J. Org. Chem.* **2013**, *2* 466–478; e) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369–375; f) M. García-Melchor, A. A. C. Braga, A. Lledos, G. Ujaque, F. Maseras, *Acc. Chem. Res.* **2013**, *46*, 2626–2634; g) J. J. Mousseau, A. B. Charette, *Acc. Chem. Res.* **2013**, *46*, 412–424; h) L. Ackermann, A. R. Kapdi, H. Potukuchi, S. I. Kozhushkov, *Handbook of Green Chemistry,* Wiley-VCH, Weinheim, **2012**, pp. 259–305; i) A. Facchetti, L. Vaccaro, A. Marrocchi, *Angew. Chem.* **2012**, *124*, 3578–3581; *Angew. Chem. Int. Ed.* **2012**, *51*, 3520–3523; j) S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936–946; k) D. Y.-K. Chen, S. W. Youn, *Chem. Eur. J.* **2012**, *18*, 9452–9474; l) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466–5492; m) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315–1345; n) S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215–1292; G. Dyker, *Handbook of C–H Transformations: Applications in Organic Synthesis*, Wiley-VCH, Weinheim, **2005**.

[7] a) B. L. Feringa, W. R. Browne, *Molecular Switches*, Wiley-VCH, Weinheim, **2011**; b) N. Ruangsupapichat, M. M. Pollard, S. R. Harutyunyan, B. L. Feringa, *Nat. Chem.* **2011**, *3*, 53–60; c) D.-H. Qu, B. L. Feringa, *Angew. Chem.* **2010**, *122*, 1125–1128; *Angew. Chem. Int. Ed.* **2010**, *49*, 1107–1110; d) B. L. Feringa, H. Wynberg, *J. Am. Chem. Soc.* **1977**, *99*, 602–603.

[8] X-ray crystallography: X-ray data were collected by using a STOE IPDS II diffractometer (graphite-monochromated $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å) by use of ω scans at −140 °C. The structure was solved by direct methods (SHELXS) and refined on F^2 using all reflections with SHELXL-97.1; see Ref. [9]. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions and assigned to isotropic displacement parameters of $1.2/1.5\,U_{eq}$(C). Face-indexed absorption corrections were performed numerically with the X-RED 2 program; see Ref. [10]. Experimental procedure: Compound **6a** (5 mg) was dissolved in Et_2O (5 mL) and stored in an *n*-hexane atmosphere. The method could be reproduced. Empirical formula: $C_{35}H_{24}O_2$, M_r: 476.54, crystal system: triclinic, space group: $P\bar{1}$; unit-cell dimensions: $a = 9.3688(4)$ Å, $b = 15.4443(8)$ Å, $c = 18.4387(10)$ Å, $\alpha = 114.625(4)°$, $\beta = 90.516(4)°$, $\gamma = 99.404(4)°$; $T = 133(2)$ K, $\lambda = 0.71073$ Å; $V = 2383.9(2)$ Å^3; $Z = 4$; $\rho_{calcd} = 1.328$ Mg m^{-3}; $\varepsilon = 0.081$ mm^{-1}; $F(000) = 1000$; crystal size: $0.500 \times 0.450 \times 0.240$ mm^3; θ range for data collection: 1.219–26.099°; index ranges: $-11 \le h \le 11$, $-19 \le k \le 18$, $-22 \le l \le 22$; reflections collected: 44852; independent reflections: 44852; completeness to $\theta = 25.242°$: 99.9%; absorption correction: numerical; max/min transmission: 0.9849/0.9654; refinement method: full-matrix least squares on F^2; data/restraints/parameters: 44852/0/668; GoF on F^2: 0.965; final *R* indices: $R1 = 0.0550$, $wR2 = 0.1326$; *R* indices (all data): $R1 = 0.0791$, $wR2 = 0.1429$; extinction coefficient: n/a; largest diff. peak/hole: 0.229/−0.149 e Å^{-3}.

[9] G. M. Sheldrick, *Acta Cryst.* **2008**, *A64*, 112–122.

[10] *X-RED*, STOE & CIE GmbH, Darmstadt, Germany, **2002**.

[11] a) J. K. Lee, H. S. Kim, S. J. Yun, Suk, *J. Photochem. Photobiol. A* **2014**, *275*, 47 – 53; b) R. Pinalli, E. Dalcanale, *Acc. Chem. Res.* **2013**, *46*, 399 – 411; c) M. Arisawa, Y. Fujii, H. Kato, H. Fukuda, T. Matsumoto, M. Ito, H. Abe, Y. Ito, S. Shuto, *Angew. Chem.* **2013**, *125*, 1037 – 1041; *Angew. Chem. Int. Ed.* **2013**, *52*, 1003 – 1007; d) C. Nunez, C. Silva Lopez, O. M. Faza, J. Fernandez-Lodeiro, M. Diniz, R. Bastida, J. L. Capelo, C. Lodeiro, *J. Biol. Inorg. Chem.* **2013**, *18*, 679 – 692; e) N. Norouzi, *Synlett* **2013**, *24*, 1307 – 1308; f) R. Sauer, P. Froimowicz, K. Schoeller, J.-M. Cramer, S. Ritz, K. Mailaender, K. Landfester, *Chem. Eur. J.* **2012**, *18*, 5201 – 5212; g) *Reviews in Fluorescence, Vol. 7* (Ed.: C. Geddes), Springer, New York, **2010**.

[12] Fluorescence spectrum: The spectrum was recorded by using an FP 6500 fluorimeter by JASCO. Light source: 150 W Xe lamp; photometric system: monochromatic light; monochromator: signal-to-noise ratio (Raman band of water, 350 nm excitation wavelength, 2 s response time, 5 nm bandwidth) of 200:1 (excitation and emission monochromator), measuring wavelength range: zero order, 220–750 nm; resolution: 1 nm (excitation and emission), wavelength accuracy: +/−1.5 nm (excitation and emission); wavelength reproducibility: +/−0.3 nm (excitation and emission); detector: photomultiplier tube (excitation and emission). Experimental procedure: Compound **6a** (980 μg) was dissolved in acetonitrile (6 mL; $c = 3.43 \times 10^{-4}$ mol L^{-1}).

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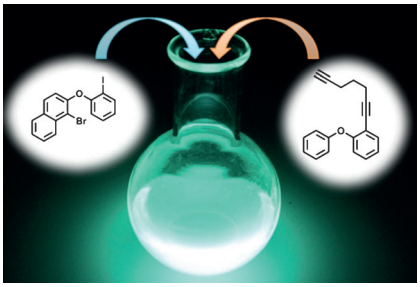
FULL PAPER

Fast Domino: We report a facile synthesis that converts simple molecules into polycyclic fluorescent dyes. The synthetic route entails a fourfold Pd-catalyzed domino Sonogashira/double-carbopalladation/C–H-activation process that enables efficient transformation of alkyne precursors into the desired products. These products exhibit strong fluorescence radiation in the blue spectral region (see figure).



Domino Reactions

L. F. Tietze, C. Eichhorst, T. Hungerland, M. Steinert*

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A Fast Way to Fluorescence: A Fourfold Domino Reaction to Condensed Polycyclic Compounds