

## Organic Chemistry

 $\pi$ -Extended Polyaromatic Hydrocarbons by Sustainable Alkyne Annulations through Double C–H/N–H ActivationElżbieta Gońka<sup>+</sup>, Long Yang<sup>+</sup>, Ralf Steinbock, Fabio Pesciaoli, Rositha Kuniyil, and Lutz Ackermann<sup>\*[a]</sup>

**Abstract:** The widespread applications of substituted diketopyrrolopyrroles (DPPs) call for the development of efficient methods for their modular assembly. Herein, we present a  $\pi$ -expansion strategy for polyaromatic hydrocarbons (PAHs) by C–H activation in a sustainable fashion. Thus, twofold C–H/N–H activations were accomplished by versatile ruthenium(II)carboxylate catalysis, providing step-economical access to diversely decorated fluorogenic DPPs that was merged with late-stage palladium-catalyzed C–H arylation on the thus-assembled DPP motif.

Since their first synthesis,<sup>[1]</sup> diketopyrrolopyrroles (DPPs) have attracted great attention from researchers from various research arenas, including optoelectronic material sciences<sup>[2]</sup> and bioimaging.<sup>[3]</sup> These inconspicuous small organic DPP molecules exhibit versatile properties ranging from low solubility, chemical resistance, outstanding stabilities and distinct colors, which render them excellent pigments.<sup>[4]</sup> N-Alkylation leads to DPPs with improved solubilities, the properties of which can be fine-tuned by the incorporation of different aromatic motifs.<sup>[3]</sup> Due to their strong electron-withdrawing ability and optical properties, DPPs are widely used as small molecules and conjugated semiconducting polymers in organic solar cells (OSCs),<sup>[2a–e, g, 5]</sup> organic field-effect transistors (OFET),<sup>[2f, 6]</sup> organic photovoltaic cells (OPVs),<sup>[7]</sup> as well as fluorescent probes,<sup>[3, 8]</sup> photocatalysts,<sup>[9]</sup> photosensitizers<sup>[10]</sup> or photothermal therapy agents,<sup>[11]</sup> promising annihilator molecules,<sup>[12]</sup> self-assembled dyes,<sup>[13]</sup> and bioconjugated hybrids.<sup>[14]</sup>

DPP derivatives with a highly decorated periphery as well as DPP-based polymers are usually obtained through convention-

al condensation reactions<sup>[4b, 15]</sup> or metal-catalyzed cross-coupling reactions with prefunctionalized substrates.<sup>[4a, 8b, 16]</sup> In comparison to the elegant efforts devoted to the modification of the DPP periphery by direct functionalization or direct arylation polymerization (DARp),<sup>[17]</sup> their de novo assembly leading to  $\pi$ -extended structures continuous to be underdeveloped, with notable recent progress by Zumbusch<sup>[18]</sup> and Würthner.<sup>[13, 19]</sup> Another possibility is represented by the introduction of an ethylene bridge between the nitrogen and the aromatic moiety, which leads to significantly  $\pi$ -expanded compounds.<sup>[20]</sup> These DPP derivatives possess sharp absorption and emission peaks, with very high molar absorption coefficients and unique fluorescence quantum yields,<sup>[20b]</sup> featuring after further modification a two-photon absorption cross-section.<sup>[20a]</sup> Very recently,  $\pi$ -extended DPP moieties were incorporated into alternating donor–acceptor copolymers resulting in a variety of low band gap copolymers.<sup>[21]</sup> Despite of these indisputable advances, thus far, these DPPs were obtained by classical N-alkylation with bromoacetaldehyde diethyl acetal, along with electrophilic aromatic substitution. Notably, this approach is hence limited to the introduction of ethylene junctions with only one substituent.

During the past decade, C–H activation has been identified as a transformative platform for various small molecule derivatizations through alkyne annulations.<sup>[22]</sup> In sharp contrast, DPP assembly and diversification by C–H functionalization or DARp have thus far largely proven elusive.<sup>[17]</sup> Within our program on sustainable C–H activation,<sup>[23, 24]</sup> we hence devised a versatile strategy for the modular assembly of DPPs in a single step by twofold C–H/N–H activation (Figure 1). Salient features of our findings include: 1) innovative ruthenium-catalyzed double C–H/N–H annulation of DPPs, 2) a  $\pi$ -expansion-strategy for PAHs, 3) access to valuable dyes with high absorption coeffi-

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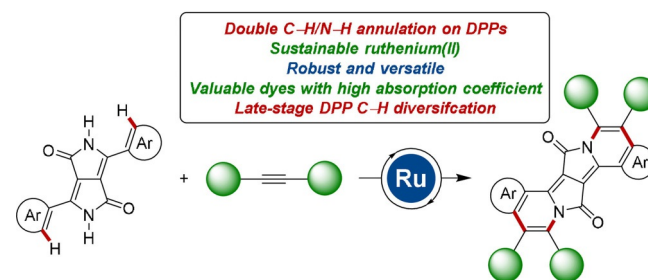
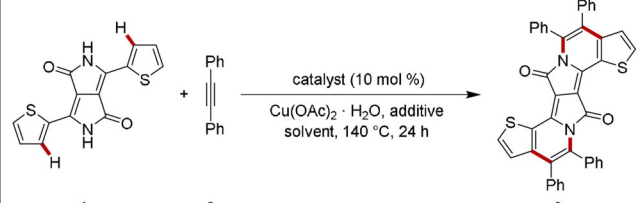


Figure 1. Double C–H/N–H activation for modular assembly of diketopyrrolopyrrole PAHs.

cients, and 4) transformative late-stage diversification by C–H arylation on the DPP motif.

We initiated our studies by probing various reaction conditions for the envisioned double C–H/N–H activation of diketopyrrolopyrrole **1a** with alkyne **2a** (Table 1, for detailed information, see Tables S1 and S2 in the Supporting Information).<sup>[25]</sup>

**Table 1.** Optimization of double C–H/N–H activation on DPP **1a**.<sup>[a]</sup>

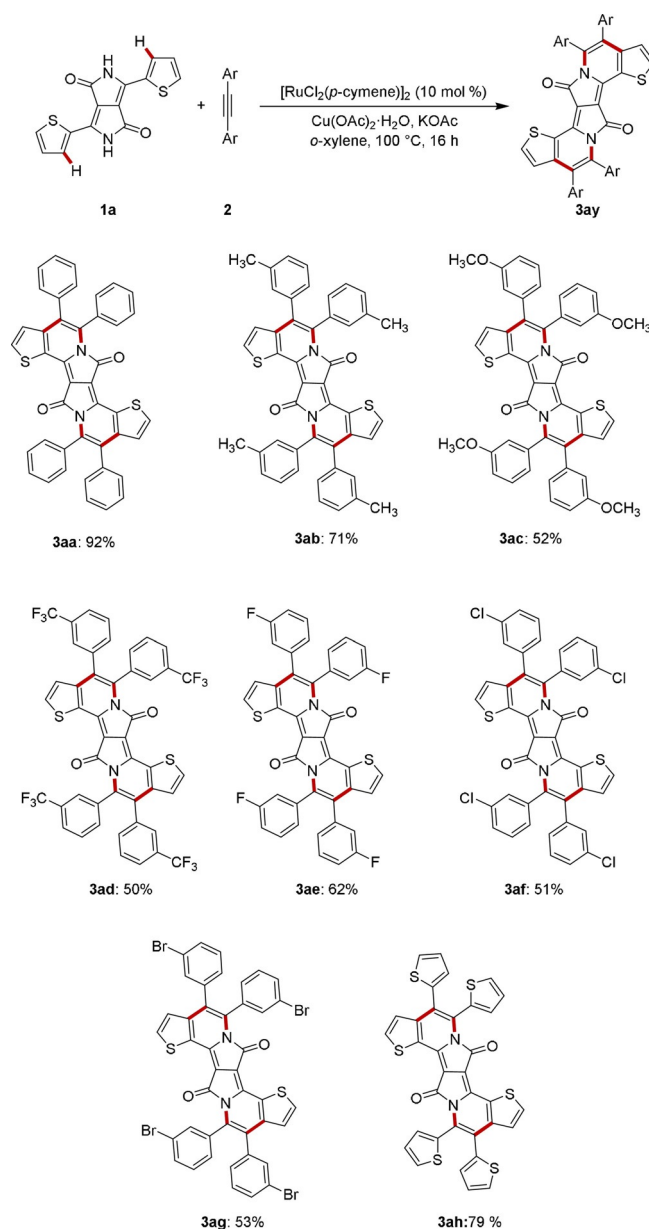


Entry	Catalyst	Additive	Solvent	Yield [%] <sup>[b]</sup>
1	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	–	<i>o</i> -xylene	35
2	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	<i>o</i> -xylene	80
3 <sup>[c,d]</sup>	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	<b><i>o</i>-xylene</b>	<b>92</b>
4 <sup>[d]</sup>	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	<b><i>o</i>-xylene</b>	<b>84</b>
5	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	DCE	70
6	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	PhMe	56
7	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	<i>t</i> AmOH	57
8	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	DMF	–
9	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	GVL	–
10	–	KOAc	<i>o</i> -xylene	–
11 <sup>[e]</sup>	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	–	<i>o</i> -xylene	–
12 <sup>[e]</sup>	[RuCl <sub>2</sub> ( <i>p</i> -cymene)] <sub>2</sub>	KOAc	<i>o</i> -xylene	–
13 <sup>[f]</sup>	Pd(OAc) <sub>2</sub>	KOAc	<i>o</i> -xylene	–
14	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	KOAc	<i>o</i> -xylene	–
15	[RhCp*Cl <sub>2</sub> ] <sub>2</sub>	KOAc	<i>o</i> -xylene	76
16 <sup>[c,d]</sup>	[RhCp*Cl <sub>2</sub> ] <sub>2</sub>	KOAc	<i>o</i> -xylene	20

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (1.00 mmol), catalyst (10 mol%), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (0.5 mmol), additive (0.25 mmol), solvent (0.2 M), 140 °C, 24 h. [b] Isolated yields. [c] 16 h. [d] 100 °C. [e] CuBr<sub>2</sub> as an oxidant. [f] 20 mol%.

Thus, moisture- and air-stable ruthenium(II) complexes emerged as the catalysts of choice, with most effective catalysis accomplished by carboxylate assistance (Table 1, entries 1–4).<sup>[26]</sup> Given the rather poor solubility of substrate **1a**<sup>[1,4b]</sup> and the aromatic character of PAH **3aa**, we next explored various solvents (entries 4–9), with *o*-xylene being superior. Control experiments confirmed the essential role of carboxylate-assisted ruthenium(II) catalysis (entries 10–11). The particularly challenging character of the twofold C–H/N–H activation was reflected by palladium and iridium catalysts failing short in delivering the desired product **3aa** (entries 13 and 14). Likewise {Cp\**Rh*<sup>III</sup>} catalysis was significantly less effective than the cost-effective ruthenium(II) manifold (entries 15 and 16).

With the optimized catalyst in hand, we tested its versatility in the double C–H/N–H activation of DPP **1a** with a variety of aryl-substituted alkynes **2** (Scheme 1). Thereby,  $\pi$ -extended PAHs were accessed from electron-rich as well as electron-deficient alkynes in an efficient manner, including sensitive tetrabromo DPP **3ag** and thiophene-rich **3ah**, which should prove instrumental for further modifications and applications of the DPPs **3**.

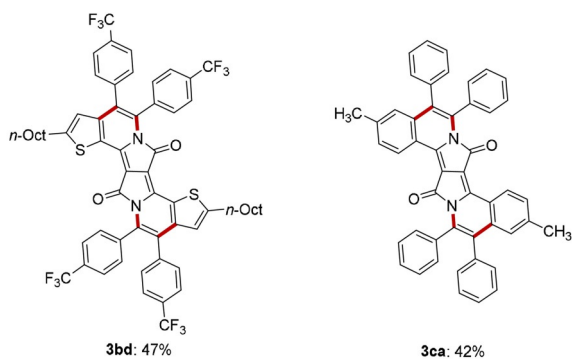
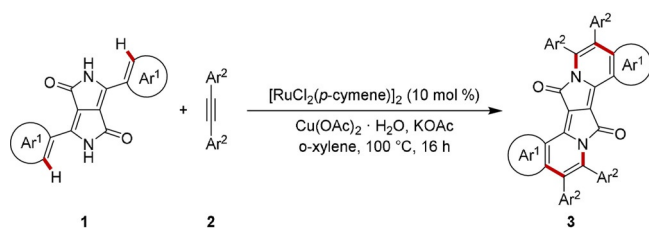


**Scheme 1.** Ruthenium(II)-catalyzed double C–H/N–H activation with aryl alkynes **2**.

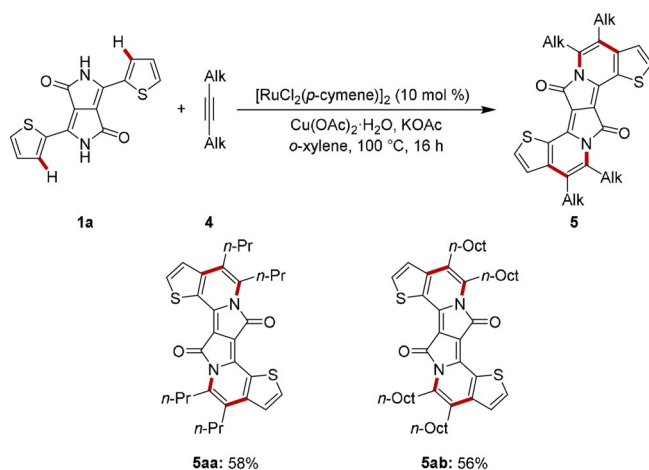
The double ruthenium-catalyzed DPP C–H/N–H activation was not restricted to unsubstituted, parent DPP **1a** (Scheme 2). Indeed, the reaction also proceeded efficiently with alkyl-substituted derivative **1b** as well as the aryl-modified-DPP **1c**, with the isolated yield of annulation product **3ca** being caused by the extremely low solubility of substrate **1c**.

Next, we evaluated alkyl-substituted alkynes **4** in the twofold ruthenium-catalyzed alkyne annulation by DPP **1a** (Scheme 3). Hence, the desired  $\pi$ -extended PAHs **5aa** and **5ab** were obtained by efficient oxidative C–H/N–H activations.

The connectivity of the annulated product **3aa** was unambiguously established by X-ray crystal diffraction analysis (Figure 2). The dihedral angle between the DPP unit and its adjacent thiophene unit was found with 6.4°, clearly showing the



Scheme 2. Double ruthenium-catalyzed C–H/N–H activations of DPPs 1.



Scheme 3. Twofold annulations of alkyl-alkynes 4 by DPP 1 a.

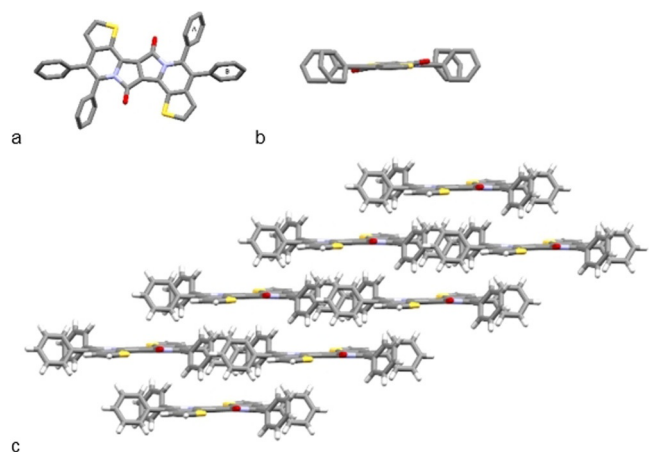


Figure 2. X-ray structure of DPP **3aa**. a) Molecular structure. b) Side view on the molecular structure, highlighting the planarity of the DPP core. c) Lamellar packing motif. Hydrogen atoms are partially omitted for clarity.

importance of the molecular tether to induce planarity, as compared with the unbridged compound.<sup>[6c]</sup> Further, the individual molecules are arranged in a lamellar packing motif,<sup>[27]</sup> which appears to be stabilized by dispersive non-covalent C–H... $\pi$  interaction between the C–H bonds of the arene motif and the thiophene unit (2.82 Å).

The optical properties of the thus-obtained novel DPP PAHs **3**, **5** and **7** were thereafter studied by detailed UV/Vis absorption and fluorescence spectroscopy (Table 2). The unprecedented-

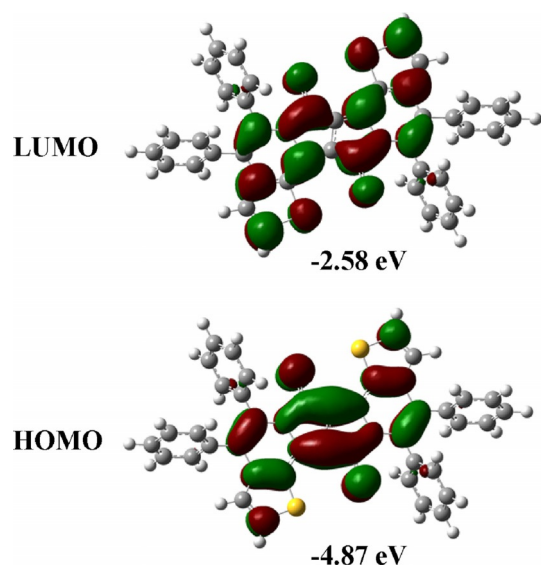
Table 2. Spectroscopic data of DPPs **3**, **5**, and **7**.

Compd.	$\lambda_{\text{abs.max}}$	$\lambda_{\text{em.max}}$	Stokes shift [ $\text{cm}^{-1}$ ]	$\epsilon_{\text{max}}$ [ $\text{M}^{-1} \text{cm}^{-1}$ ]
<b>3aa</b>	633	645	293	78677
<b>3ab</b>	635	645	244	52083
<b>3ac</b>	635	646	268	71946
<b>3ad</b>	632	641	222	66051
<b>3ae</b>	631	640	223	47269
<b>3af</b>	633	644	270	76626
<b>3ag</b>	633	643	246	76107
<b>3ah</b>	636	646	243	25878
<b>3bd</b>	637	644	158	11431
<b>3ca</b>	604	613	270	92095
<b>5aa</b>	630	639	223	71598
<b>5ab</b>	631	642	272	84835
<b>7</b>	680	694	296	53634

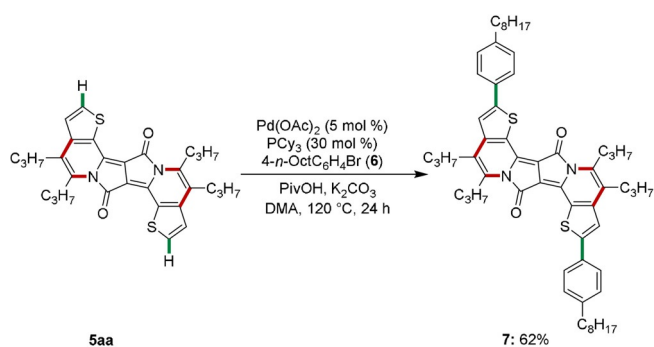
ed DPPs exhibited very intense absorption in the UV and visible region, with absorption maxima between maxima between 600–680 nm OR maxima between 600–640 nm for the annulation products **3** and **5**, which results in an intense blue to purple color. The absorption maximum in all synthesized derivatives is bathochromically shifted in comparison with the previously synthesized, unsubstituted compounds,<sup>[20b]</sup> whereas both Stokes shift and absorption coefficient are comparable. Interestingly, the highest absorption coefficients were obtained for the *p*-tolyl-DPP derivative **3ca**, while the largest Stokes shift was observed for thiophene-DPP derivative **3aa** and **7**.

To investigate further the electronic structure of the DPPs **3**, we performed computational DFT studies for product **3aa** at the B3LYP-D3(BJ)/6–311 + G(d,p) + SMD(*o*-Xylene) level of theory (Figure 3).<sup>[25]</sup> Our calculations showed that the HOMO is delocalized over the DPPs core and the ethylene bridge, whereas the LUMO is evenly localized on all condensed rings. Moreover, our TD-DFT calculations, performed at the same level of theory, highlighted an optical gap ( $E_{\text{opt}}$ ) of 2.02 eV. Our computed absorption spectrum is in good qualitative agreement with the experimental data.<sup>[25]</sup>

Finally, we became attracted by further late-stage functionalization of PAH **3am** in terms of the introduction of two aryl motifs<sup>[17a]</sup> at the alpha positions of the thiophenes (Scheme 4). Thus, the desired assembly of octylphenyl-substituted DPP **7** was realized by palladium-catalyzed twofold C–H arylations. It is noteworthy that the C–H activation-based incorporation of two aromatic moieties drastically shifted both the absorption and the emission maxima into the NIR region, which was mirrored by the green color of PAH **7**.



**Figure 3.** Energies and shapes of frontier orbitals (HOMO and LUMO) of **3aa** calculated at the B3LYP-D3(BJ)/6-311+G(d,p)+SMD(*o*-Xylene) level of theory.



**Scheme 4.** Late-stage PAH diversification by double C–H arylations. Cy = cyclohexyl; DMA = dimethylacetamide; PivOH = pivalic acid.

In summary, we have devised an enabling strategy for the assembly of  $\pi$ -extended DPPs. Thus, ruthenium(II)-catalyzed double C–H/N–H activation allowed for the synthesis of novel, diversely-decorated DPP derivatives in a step-economical manner. The novel DPPs were fully characterized, including spectroscopy, XRD and DFT computation. The twofold alkyne annulation was furthermore merged with C–H arylations of the thus obtained  $\pi$ -extended PAHs to furnish DPPs with absorption and emission maxima shifted into the NIR region. Our findings should prove invaluable for applications to optoelectronics, material sciences and live cell imaging.<sup>[28]</sup>

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## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** annulation • C–H activation • diketopyrrolopyrroles • polyaromatic hydrocarbons • ruthenium

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