
# A New Synthetic Route to 5,6,11,12-tetraarylethynyltetracenes

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# A New Synthetic Route to 5,6,11,12-tetraarylethynyltetracenes

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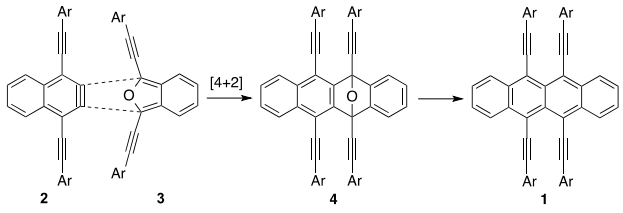
**A new synthetic route to 5,6,11,12-tetrakis(arylethynyl)tetracenes, π-extended rubrenes, was developed via [4+2] cycloadditions of dialkynylisobenzofuran and 1,4-naphthoquinone. Introduction of arylethynyl groups by double nucleophilic additions to tetracenequinone gave sterically congested (arylethynyl)tetracenes after reductive aromatization. The photophysical properties of the newly prepared π-conjugated molecules are also evaluated.**

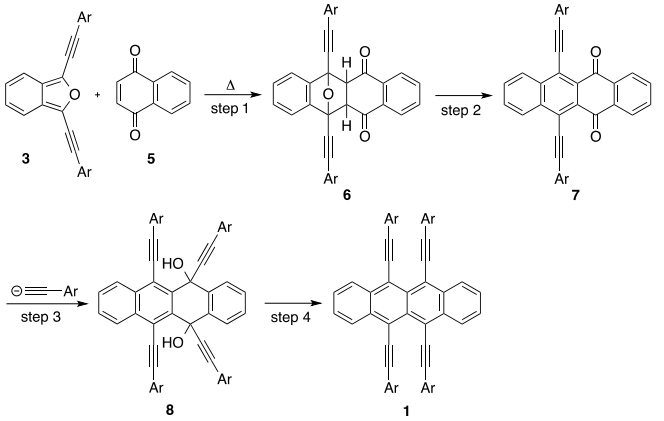
We previously reported a preparation of 5,6,11,12-tetraarylethynyltetracene **1**, a new class of π-extended rubrenes, via [4+2] cycloaddition of dialkynylnaphthalyne **2** and dialkynylisobenzofuran **3** (Scheme 1).[1,2] In this reaction, two alkynyl groups onto the naphthalyne **2** can lower the LUMO energy, allowing the practical construction of the sterically overcrowded structure through their efficient HOMO–LUMO interaction.




**Scheme 1** The first syntheses of π-extended rubrenes **1** via [4+2] cycloaddition of naphthalyne and isobenzofuran

This approach, however, has a problem in that the yield of the aromatization (**4**→**1**) is low or moderate owing to the unexpected reactivities derived from the closely located *peri*-ethynyl groups in epoxytetracene **4** under the acidic conditions.[3]

To solve this problem, we focused on developing a new synthetic route to π-extended rubrene **1** using dialkynylisobenzofuran **3** as a reactive platform.[4,5] Our second approach is consisting of four-step syntheses, which is depicted in Scheme 2.[6] In the first step, the [4+2] cycloaddition of dialkynylisobenzofuran **3** and 1,4-naphthoquinone (**5**) gives the cycloadduct **6**, which is converted to the tetracenequinone **7** by aromatization (step 2). Subsequent introduction of two alkynyl groups by double nucleophilic additions of alkynyl anions (step 3), and reductive aromatization of the resulting diol **8** would produce the target compound **1** (step 4). Along these lines, we now report an efficient synthetic access to π-extended rubrenes possessing various arylethynyl groups at the *peri*-positions. Moreover, photophysical properties of the newly prepared poly-ethynylated tetracenes are evaluated. Also described is the application of the parent compound **1a** to a cellular imaging agent.

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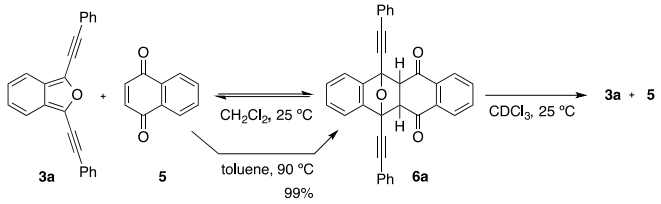
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

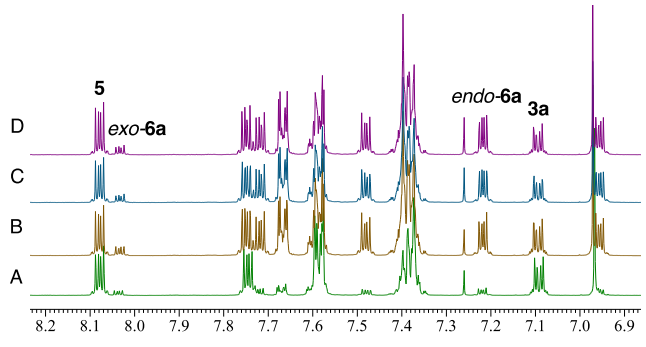
**Scheme 2** New synthetic route to π-extended rubrenes **1**

Scheme 3 shows the [4+2] cycloaddition of dialkynylisobenzofuran. Upon mixing of isobenzofuran **3a** and naphthoquinone **5** ($CH_2Cl_2$, r.t.), the new spot corresponded to the cycloadduct **6a** was observed by TLC. Further reaction at same temperature, however, did not completely consume the starting materials **3a** and **5**, indicating their equilibrium with the cycloadduct **6a**. Indeed, $^1$H NMR analysis revealed that the cycloadduct **6a** including endo- and exo-isomer was readily formed after dissolving the isobenzofuran **3a** and naphthoquinone **5** in $CDCl_3$ at room temperature (see A in Figure 1). After 7 h, the ratio of **3a**, **5**, exo-**6a**, and endo-**6a** almost became constant (see D in Figure 1). The stereochemistry of the exo-**6a** and endo-**6a** was tentatively assigned by consideration of the chemical shift of each methine proton.[7]




**Scheme 3** [4+2] Cycloaddition between isobenzofuran **3a** and 1,4-naphthoquinone (**5**)

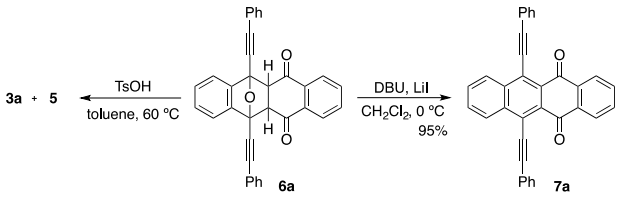
After further study on this [4+2] cycloaddition, we were pleased to find that solvent choice is crucial to produce the high yield of the cycloadduct **6a**: when the above mentioned reaction was performed in toluene at 90 °C, the [4+2] cycloadduct **6a** gradually precipitated from the solution due to its low solubility in toluene, affording the essentially pure product **6a** almost in quantitative yield (Scheme 3). Interestingly, the endo isomer **6a** was solely produced under this conditions. By dissolving in $CDCl_3$ (25 °C, 26 h), the cycloadduct **6a** again underwent the cycloreversion to give the dialkynylisobenzofuran **3a** and 1,4-naphthoquinone (**5**).[8]




a) A: 5 min, B: 2 h, C: 7 h, D: 15 h

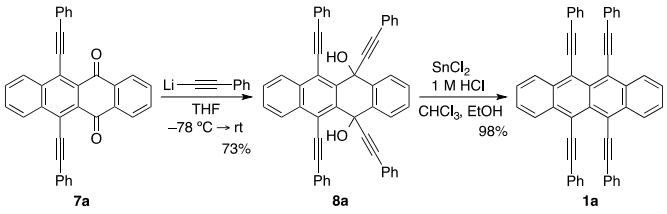
**Figure 1** [4+2] Cycloaddition between isobenzofuran **3a** and 1,4-naphthoquinone (**5**) monitored by NMR.

Scheme 4 shows the conversion of the [4+2] cycloadduct **6a** to tetracenequinone **7a**. Upon heating of cycloadduct **6a** in the presence of TsOH at 60 °C, the cycloreversion occurred quickly, and the aromatized product **7a** was not obtained at all.[9,10] On the other hand, treatment of the cycloadduct **6a** with LiI and DBU at low temperature ($CH_2Cl_2$, 0 °C)[11] underwent the clean aromatization without invoking the cycloreversion to give the tetracenequinone **7a** in 95% yield.

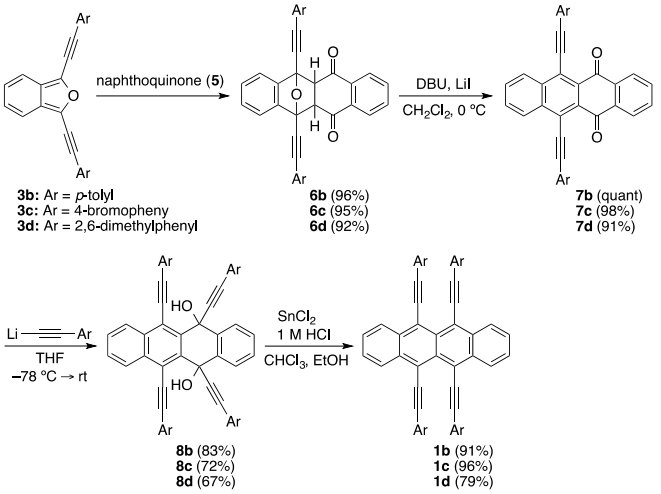



**Scheme 4** Aromatization of cycloadduct **6a** to tetracenequinone **7a**

Further transformation of the tetracenequinone **7a** to π-extended rubrene **1a** was achieved through double nucleophilic additions of phenylethynyllithium, followed by $Sn^{II}$-mediated reductive aromatization (Scheme 5). Importantly, the nucleophilic addition of alkynyllithium to **7a** occurred cleanly by warming the reaction to room temperature, in spite of the high steric hindrance between incoming nucleophile and proximal alkynyl groups.




**Scheme 5** Transformation of tetracenequinone **7a** to π-extended rubrene **1a**




**Scheme 6** Preparation of π-extended rubrenes **1b–1d**

In a similar manner, the substituted derivatives **1b** and **1c**, having four *p*-tolylethynyl or (4-bromophenyl)ethynyl groups at both *peri*-positions, were efficiently synthesized by this four-step sequence including the tetracenequinones **7b** and **7c** as key intermediates (Scheme 6).

It should be noted that the developed method has high synthetic potential in that the sterically congested derivative **1d** possessing four 2,6-xylylethynyl groups on the tetracene core was easily accessible in good yield. This is a sharp contrast from our previous method by acid-promoted aromatization of the epoxy tetracene **4d** (Ar: 2,6-xylyl), where the product **1d** was obtained in poor yield, and a sizable amount of furan (structure not shown) was produced.[1]

To evaluate the photophysical properties, UV–Vis spectra of π-extended rubrenes **1a**–**1d** were measured in chloroform (Figure 2). The π-extended rubrene **1a** has its absorption maximum at 640 nm, which was greatly red-shifted over 100 nm from that of the parent rubrene, indicating effective π-extension by the existence of four phenylethynyl groups on the tetracene core. The π-extended rubrenes **1b** and **1c** with para-substitution denoted the similar tendency of **1a**, whereas the absorption maximum of the sterically congested derivative **1d** was slightly blue-shifted (623 nm).

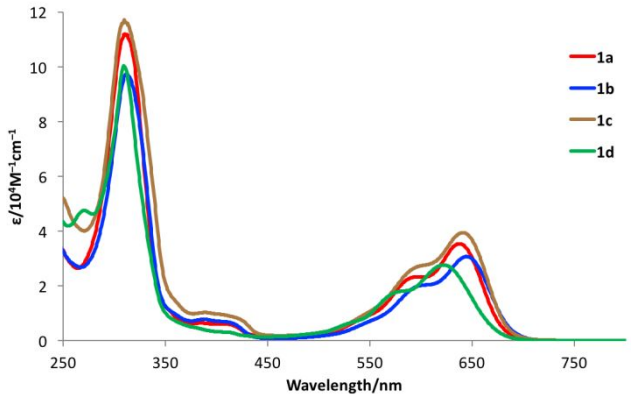



**Figure 2** UV–Vis absorption spectra of π-extended rubrenes **1a**–**1d**.

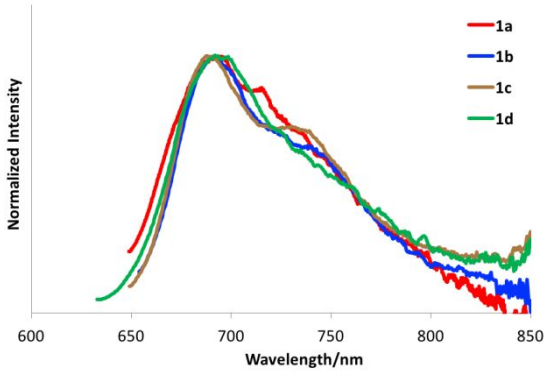



**Figure 3** Fluorescence spectra of π-extended rubrenes **1a**–**1d**.

Fluorescent spectra were also measured in chloroform (Figure 3). The π-extended rubrenes **1a**–**1d** showed the fluorescent maximum peaking at around 690 nm, which were excited at their absorption maximum. Larger Stokes shift was observed in **1d** (1620 $cm^{-1}$) compared to that of **1a** (1200 $cm^{-1}$). The absolute fluorescent quantum yields of these π-extended derivatives were nearly 10%, which were lower than that of the parent rubrene.

Finally, preliminary investigation of cellular imaging using π-extended rubrene was performed by treating the HeLa cells with **1a** for 30 min at 37 °C. Fluorescence signals from cells upon excitation with 620 nm indicate a future applicability of π-extended rubrene as bioimaging probe.

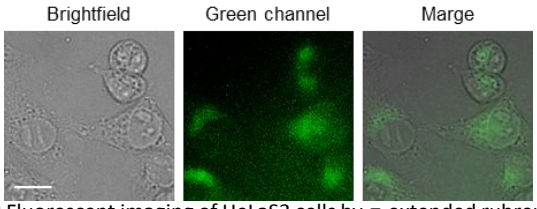



**Figure 4** Fluorescent imaging of HeLaS3 cells by π-extended rubrene. The cells were treated with 100 μM of **1a** for 30 min at 37°C and analyzed by fluorescent microscopy. Green channel: $\lambda_{em}$ = 620 nm, $\lambda_{ex}$ = 700 nm. Scale bar: 20 μm.

## Conclusions

In conclusion, [4+2] cycloaddition of dialkynylisobenzofuran and 1,4-naphthoquinone allowed rapid construction of alkynylated tetracenequinones, which were amenable to transformation en route to tetrakis(arylethynyl)tetracenes. Further study on application of these attractive π-conjugated molecules to organic electronics materials and fluorescent probes are under active investigation in our laboratories.

## Acknowledgement

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## Conflicts of interest

There are no conflicts to declare.

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8 The perfect endo selectivity observed in the [4+2] cycloaddition of isobenzofuran **3a** and naphthoquinone **5** is presumably due to the lower solubility of the endo cycloadduct **6a** in toluene than that of the exo cycloadduct **6a**. Therefore, the endo cycloadduct **6a** was selectively precipitated from the solution under the equilibrium between the starting materials and the cycloadducts. In a similar manner, the endo cycloadducts **6b**–**6d** were obtained as a single stereoisomer by precipitation owing to their poor solubility with EtOH or heptane. For details, see Supporting Information.

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