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Intramolecular benzoallene–alkyne cycloaddition initiated by site-selective S_N2' reaction of epoxytetracene en route to π -extended pyracylene

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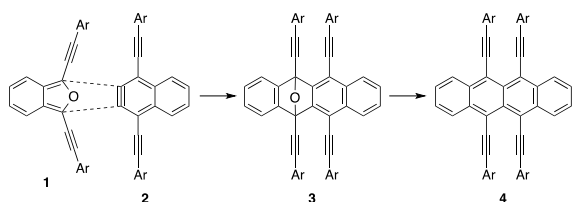
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Hydrogen halide promoted cascade reaction of epoxytetracene to halo-benzoindenotetracene including benzoallene intermediate was developed. The remaining two alkynyl groups in benzoindenotetracene was further reacted with norbornadiene or aryl amine through the transition metal-catalyzed cyclization to give π -extended pyracylene derivatives.

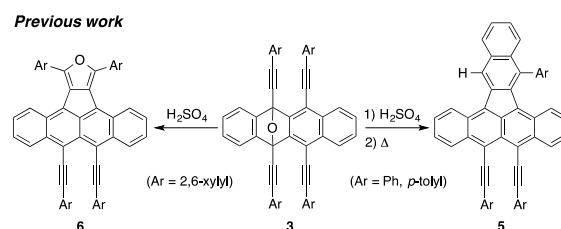
Introduction of π -conjugated substituents at the *peri* position onto the polyacene core would induce a distortion, which leads to express unique physical properties by the positive or negative π - π interaction.^{1,2} Another interesting feature existed in this distorted π -conjugated structure is potentially high reactivities caused by the closely located multiple bonds at the *peri* position.³ In this context, we previously reported an efficient synthetic access to 5,6,11,12-tetrakis(phenylethynyl)tetracene (**4**), a new class of π -extended tetracenes, via the [4+2] cycloaddition of dialkynylisobenzofuran **1** and dialkynylnaphthalene **2**.^{4,5}



Scheme 1 A synthetic route to π -extended rubrene **4**.

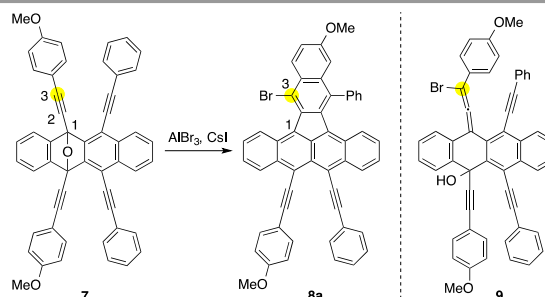
Initial study on the reactivities inherent in the *peri*-ethynyl-substituted tetracene derivatives **3** and **4** led to develop the two reactions, 1) thermal isomerization of π -extended rubrene

4 to benzoindenotetracene **5** (**3**→**4**→**5**), and 2) acid promoted cyclization of epoxytetracene **3** to furan **6** (**3**→**6**) (Scheme 2).⁶



Scheme 2 Two reaction modes of *peri*-ethynyl-substituted epoxytetracene **3**.

Upon further investigation along these lines, we accidentally found that epoxytetracene **7** underwent cascade reaction by treatment with $AlBr_3$ and CsI , affording the bromo-benzoindenotetracene **8a** in low yield (Scheme 3).⁷ The product **8a** might be formed by site-selective S_N2' attack of bromide ion at C₃ position in epoxytetracene **7** and subsequent intramolecular [4+2] cycloaddition of benzoallene intermediate **9**.



Scheme 3 Lewis acid promoted cascade reaction of epoxytetracene **7** to benzoindenotetracene **8**.

Based on this knowledge, we developed the acid-promoted cascade reaction of epoxytetracene **3a** to halo-benzoindenotetracene **11**. In this successive process, hydrogen halide served as an initiator for site-selective S_N2' reaction to epoxytetracene **3a**, thus generating benzoallene intermediate **10**, which, in turn, underwent intramolecular [4+2] cycloaddition to give halo-benzoindenotetracene **11**. Further

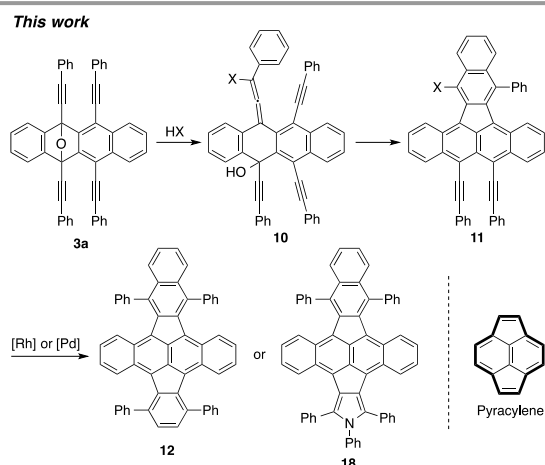
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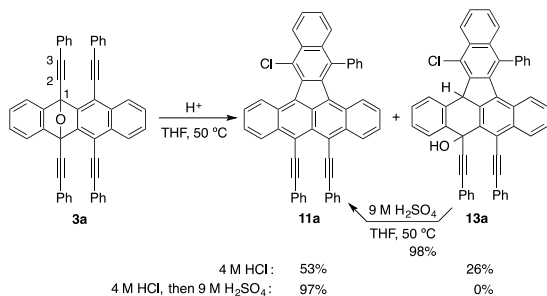
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

transformation through transition metal-catalyzed coupling reaction, followed by cyclization of **11** produced novel π -extended pyracylene derivatives **12** or **18** with potentially unique properties based on the 12π -antiaromatic pyracylene framework (Scheme 4).⁸



Scheme 4 Intramolecular benzoallene-alkyne cycloaddition of **3a** and transition metal-catalyzed coupling reaction and cyclization of **11**.

Scheme 5 shows the cascade reaction of epoxytetracene **3a**. Upon treatment of **3a** with 4 M HCl (THF, 50 °C, 10 h), S_N2' attack by chloride ion occurred site-selectively at C₃ position, and subsequent intramolecular cyclization of the resulting benzoallene intermediate **10a** (X=Cl, see Scheme 4) gave chloro-benzoindenotetracene **11a** and dihydrobenzoindenotetracene **13a**⁹ in 53% and 26% yields, respectively.



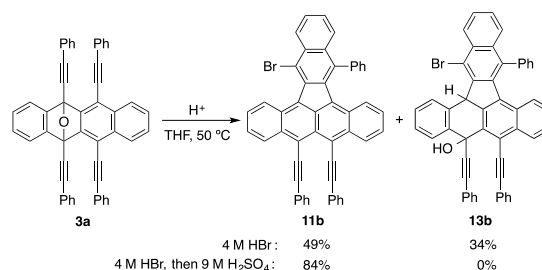
Scheme 5 Acid promoted cascade reaction of epoxytetracene **3a** to benzoindenotetracene **11a**.

In this successive process, prolonged reaction and/or higher reaction temperature under similar conditions did not promote the formation of the indenotetracene **11a**. On the other hand, use of stronger acid (9 M H₂SO₄) was effective for dehydration of **13a** to **11a** (98% yield). Based on this result, the epoxytetracene **3a** was sequentially treated with 4 M HCl and 9 M H₂SO₄ (THF, 50 °C) to give **11a** in 97% yield. These results indicated the two possible routes for the formation of **11a** from the epoxytetracene **3a** (vide infra).

The structure of **11a** was elucidated by X-ray crystal structure analysis after recrystallization from chloroform/hexane (Figure S4).¹⁰ There are two independent half molecules in the unit cell, and each molecule adopts different conformations. The common feature of these molecules is a twist conformation in

the tetracene and naphthalene moieties. The end-to-end twist angles of tetracene and naphthalene planes are 16.4° and 10.8° for Mol-A, and 4.1° and 14.4° for Mol-B. In addition, the two ethynyl units are oriented aside from each other due to the steric π -congestions. The distances of C₂₉...C₃₂ and C₃₀...C₃₃ in Mol-A are 2.84 Å and 3.31 Å, and 2.87 Å and 3.43 Å for Mol-B. The steric repulsion of two alkynyl groups was also evaluated by the torsion angle (C₂₉-C₁₅-C₁₇-C₃₂ = 12.1° for Mol-A and C₂₉-C₁₅-C₁₇-C₃₂ = 2.9° for Mol-B). Moreover, the *sp* carbon atoms of the acetylene units were deformed from linearity (e.g. C₁₅-C₂₉-C₃₀ = 172.2° for Mol-A and C₁₇-C₃₂-C₃₃ = 171.1° for Mol-B).

Further examination of the reactivity of **3a** with Brønsted acids revealed that 4 M HBr also promoted the cascade reaction, affording the cyclized product **11b** in 49% yield, accompanied by a sizable amount of dihydrobenzoindenotetracene **13b** (Scheme 6). Again, sequential treatment of **3a** with 4 M HBr and 9 M H₂SO₄ cleanly gave the aromatized product **11b** in 84% yield without producing the dihydro-derivative **13b**.¹¹

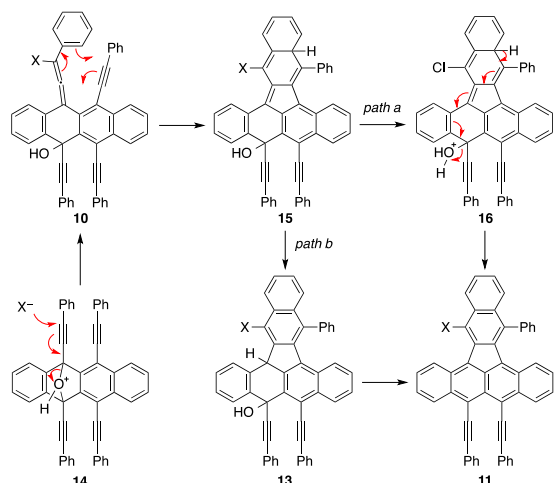


Scheme 6 HBr promoted cascade reaction of epoxytetracene **3a** to bromo-benzoindenotetracene **11b**.

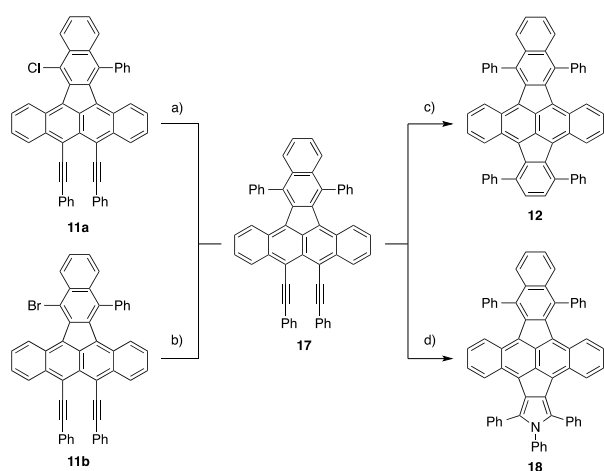
The plausible mechanism for the formation of halo-benzoindenotetracene **11** is depicted in Scheme 7. In the first step, site-selective S_N2' attack of halide ion to protonated epoxytetracene **14** gave halo-allene intermediate **10**, which underwent intramolecular Diels-Alder reaction, affording the heptacyclic alcohol **15**. Subsequent aromatization of **15** to the final product **11** has two routes. The first is the direct pathway by the dehydrative aromatization of the protonated intermediate **16** (path a). The second is stepwise process via 1,5-hydrogen shift of the polycycle **15** to dihydrotetracene **13**, followed by its dehydrative aromatization (path b). As evidenced by the acid-promoted aromatization of **3a** (vide supra), the dehydration from **13** to **11** was much slower than that from **16**.

The halo-benzoindenotetracene **11**, thus obtained, is synthetically attractive since both halogen atom introduced in the naphthalene moiety and proximal alkynyl groups at *peri*-position can be used for further functionalization by transition metal catalysed coupling reaction and annulation, leading to the selective synthesis of highly condensed aromatic compounds (Scheme 8). Indeed, Suzuki-Miyaura coupling of **11a** with Pd₂(dba)₃ in the presence of IMes-HCl gave the diphenyl-benzoindenotetracene **17** in 86% yield. Bromide **11b** also served as a good substrate in coupling reaction to give **17** in high yield. Further π -extension by ring-construction using the proximal alkynyl groups in **17** was realized by the Rh

catalyzed [2+2+2] cycloaddition with norbornadiene to give pyracylene **12** in 81% yield.^{12–14} Pyrrole-containing π -extended pyracylene **18** was also prepared by treatment of **17** with aniline in the presence of PdCl₂ and NEt₃.¹⁵ These cyclopenta-fused polycyclic aromatics, thus obtained, have attracted substantial interest since pyracylene exhibits a considerable antiaromatic contribution to its electronic structure as well as a high electron affinity derived from its 12 π -electron framework.⁸



Scheme 7 Plausible reaction mechanism for the formation of halo-benzoindenetetracene **11**



- a) PhB(OH)₂, Pd₂(dba)₃, IMes-HCl, Cs₂CO₃, toluene, 80 °C, 86%
 b) PhB(OH)₂, Pd(PPh₃)₄, K₂CO₃, 1,4-dioxane, 80 °C, 96%
 c) 2,5-norbornadiene, [Rh(cod)₂Cl]₂, toluene, 80 °C, 81%
 d) PhNH₂, PdCl₂, NEt₃, DMSO, 100 °C, 45%

Scheme 8 Suzuki–Miyaura cross coupling of **11** and transition metal catalyzed cyclization of **17**.

To evaluate electronic properties, the UV–visible absorption spectra and the cyclic voltammograms of **17**, **12**, and **18** were measured (Figures 1 and 2). The absorption spectrum of compound **12** showed the longest wavelength absorption at $\lambda_{\text{max}} = 710$ nm, which is red-shifted by 31 nm and 70 nm in comparison with that of **17**, and π -extended tetracene **4** (Ar = Ph), respectively. Moreover, it is remarkably red-shifted by nearly 100 nm with respect to that of tetrabenzo-fused

pyracylene,^{8c} indicating effective π -extension by the peripheral substituents. Pyrrole-fused derivative **18** exhibited a similar absorption band ranging from 550 nm to 750 nm and has its absorption maximum at 707 nm. Time-Dependent DFT calculations suggested the longest wavelength of **12** is predominantly contributed from HOMO→LUMO transition at 711 nm with oscillator strength $f = 0.40$, which is consistent with experimental data. The cyclic voltammograms of **12**, **17**, and **18** were recorded in degassed THF (1.0 mM) using *n*-Bu₄NPF₆ as a supporting electrolyte. In the reduction process, compounds **12** and **17** exhibited two reversible waves ($E_{1/2} = -1.34$ V and -1.68 V for **12**; $E_{1/2} = -1.39$ V and -1.74 V for **17**), reflecting low-lying LUMO energy level derived from their high electron affinities. In the oxidation process, irreversible waves were observed ($E_{\text{onset}} = +0.31$ V for **12**; $E_{\text{onset}} = +0.34$ V for **17**). The electrochemical gap for **12** and **17** are 1.65 eV and 1.73 eV, respectively, which are in excellent agreement with the HOMO–LUMO energy gaps obtained from the onsets of their absorption spectra (748 nm, 1.66 eV for **12**; 715 nm, 1.73 eV for **17**). Pyrrole-containing derivative **18** showed two major reduction waves ($E_{1/2} = -1.54$ V and -1.93 V) and irreversible oxidation wave ($E_{\text{onset}} = +0.15$ V), which are negatively shifted compared to that of **12**. This difference was due to the existence of the electron donating pyrrole moiety in **18**. The energy gap is in good agreement with the onsets of the absorption spectra (744 nm, 1.67 eV).

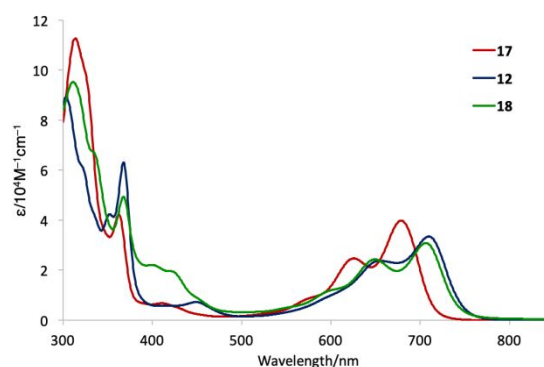


Figure 1 UV–Vis absorbance spectra of **12**, **17**, and **18** in toluene.

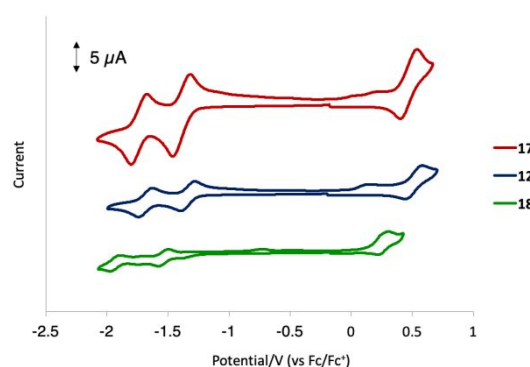


Figure 2 Cyclic voltammograms of **17**, **12**, **18** in THF.

To gain an insight into the aromatic character, the nucleus-independent chemical shift (NICS) were calculated for compounds **17**, **12**, and **18** (B3LYP/6-31G*). The values of the

two pentagonal rings in **12** are more positive (+8.4, +8.5) than that of **17** (+3.7), showing enhanced antiaromatic character after ring formation (Figure 3). Similar tendency was observed for the pentagonal ring in **18**, although the value of pentagonal ring (+5.8) fused to the naphthalene ring decreased.

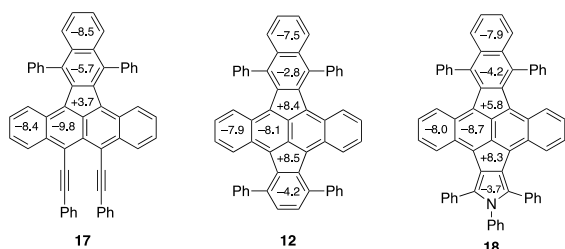


Figure 3 NICS(0) values for compounds **17**, **12**, and **18** calculated at the GIAO-B3LYP/6-31G*.

Conclusions

Brønsted acid promoted cascade reaction of epoxytetracene to halo-benzoindenotetracene was developed. The key process was initial site-selective S_N2' reaction to epoxytetracene, which selectively generated benzoallene-alkyne intermediate. Further transformations including ruthenium-catalyzed [2+2+2] cycloaddition with norbornadiene or arylamine produced π -extended pyracylene. Further studies on developing the unique reactivities inherent in the *peri*-ethynyl-substituted polyacene derivatives are currently underway in our laboratory.

Acknowledgement

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Conflicts of interest

There are no conflicts to declare.

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- Iodo-benzoindenotetracene **8b** was also included in the products. The structure of **8a** was determined by X-ray analysis after recrystallization. For details, see supporting information.
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- The structure was determined by 2D-NMR spectroscopy (HMBC, HMQC). For details, see the Supporting Information.
- $C_{50}H_{27}Cl$, MW = 663.16, 0.55 x 0.10 x 0.08 mm, Triclinic, space group $P-1$, $Z = 4$, $T = 200(2)$ K, $a = 10.264(5)$ Å, $b = 14.861(8)$ Å, $c = 24.721(11)$ Å, $\alpha = 92.409(6)^\circ$, $\beta = 91.727(7)^\circ$, $\gamma = 104.223(7)^\circ$, $V = 3649(3)$ Å³, $\lambda(\text{Mo K}\alpha) = 0.71075$ Å, $\mu = 0.139$ mm⁻¹. A total of 42434 reflections were measured and 16719 were independent. Final $R_1 = 0.0666$, $wR_2 = 0.2024$ (11364 refs; $I > 2\sigma(I)$), and GOF = 1.070 (for all data, $R_1 = 0.0945$, $wR_2 = 0.2493$).
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