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<td>Saino, Naoko; Kawaji, Tsuyoshi; Ito, Taichi; Matsushita, Yuko; Okamoto, Sentaro; 岡本 专太郎</td>
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Synthesis of substituted anthracenes, pentaphenes and trinaphthylenes via alkyne cyclotrimerization reaction

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Novel substituted anthracene derivatives including annulated pentaphenes and trinaphthylenes were synthesized through alkyne [2 + 2 + 2] cycloaddition as a key reaction.
Synthesis of substituted anthracenes, pentaphenes and trinaphthylenes via alkyne cyclotrimerization reaction

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Abstract—The [2 + 2 + 2] cycloaddition reaction of 1,6-dienes 3 with 4-aryl-2-butyn-1-ols 4 and the following oxidation of the resulting benzyl alcohols to the aldehydes 1 and then treatment with an acid catalyst provided annulated anthracenes 2 in good yields. © 2011 Elsevier Science. All rights reserved

Anthracene and its derivatives are some of the most versatile polycyclic aromatic compounds. Thus, they have received wide utilities as a chromophor for sensors and markers in biological or supramolecular systems, a key species in the design of luminescent materials, a photochromic molecule by their photo-induced cycloaddition/cycloreversion and a core structure of organo-electronic materials. Therefore, various methods for construction of anthracene framework have been developed, which include Friedel-Crafts reaction, aromatic cyclodehydration, Elbs reaction, Bradsher-type reaction of diarylmethanes and [4+2] cycloaddition reactions with naphthoquinones, quinomethanes, radialenes or benzenes. In addition, several transition metal-mediated or catalyzed cyclotrimerization processes have been reported for the rapid assembly of acenes: Ni- and Co-catalyzed or Zr-mediated alkyne-cyclotrimerization reactions via metallacycles derived from 1,2-dipropargylaromatic compounds and Pd-catalyzed benzene cyclotrimerization. These methodologies are useful for preparation of higher polycyclic aromatic hydrocarbons (PAHs) and also synthesis of acenes having a heteroaromatic substructure(s).

Based on our results of developing a highly practical procedure for synthesizing substituted benzenes by the [2 + 2 + 2] alkyne-cyclotrimerization which is catalyzed by a CoCl2·6H2O/Zn reagent in the presence of an appropriate ligand, we planned a two-step preparation of benzyl aldehydes 1, which are the substrate of Bradsher-type cyclization-aromatization reaction, by the cycloaddition of diynes 3 and 4-aryl-2-butyn-1-ols 4 and the following oxidation (Scheme 1). We have shown that the propargyl alcohols 4 are good substrate for the selective cross-coupling with diynes 3, owing to their coordination effect of the propargyl oxygen to the metal center in an active catalyst. Herein we report the results of the study for the three-step synthesis of substituted anthracenes 2 from alkyne starting materials, which were applied to synthesis of substituted pentaphenes and trinaphthylenes.

Synthesis of 4-aryl-2-butyn-1-ols 4 required for the synthesis was illustrated in Scheme 2. Compounds of the type 4 were synthesized by the cobalt-catalyzed coupling reaction of benzyl chlorides with trimethylsilylthethylmagnesium bromide, developed by us, and the following protodesilylation and hydroxymethylation reactions. Similarly, bis-propargyl alcohol 4c was prepared from 1,3-dichloromethylbenzene in 51% overall yield.

With compounds 4a-c, we carried out three-step synthesis of anthracenes 2 from diynes 3 and 4-aryl-2-butyn-1-ols 4 (Scheme 3). Thus, to a mixture of 3, 4 (1.18 equiv.) and Zn powder (10 mol%) in THF was added a solution of 2-(2,6-diisopropylamino)methylpyridine (Dipimp, 6 mol%) and CoCl2·6H2O (5 mol%) in THF at room temperature and the
mixture was stirred at ambient temperature overnight. The mixture was filtered through a pad of Celite with ether. The resulting adducts were converted to the corresponding aldehydes by treatment with PCC/Celite in CH₂Cl₂ at room temperature, which were successively treated with a catalytic amount of CF₃SO₃H in CH₂Cl₂ at reflux temperature for 1 h to provide the desired anthracenes in good yields. Anthracenes having a carbocyclic as well as heterocyclic saturated ring which was originated from tether structure of diynes were obtained. Introduction of substitution(s) at the 1 and 4 positions of as the case of was readily carried out by use of the corresponding substituted diynes. Substituent(s) at the 5~8 position(s) may be possible by using the corresponding as exemplified by synthesis of .

Scheme 2. Preparation of 4.

Scheme 3. Three-step synthesis of anthracenes from 3 and 4.

Scheme 4 shows an efficient synthesis of pentaphenes via a tandem cycloaddition reaction starting from dipropargylic compound 4c. With use of 4e as a mono-alkyne counterpart, the cycloaddition of 1,6-diyne 3a proceeded in a tandem fashion to yield bis-benzylic alcohol 5ac. The sequential reactions of oxidation/acid-catalyzed cyclization converted the resulting 5ac smoothly to bis-annulated pentaphene 2ac. Cyclization/aromatization of dialdehyde 1ac could proceed regioselectively through a possible intermediate i, illustrated in Scheme 4, to provide pentaphene 2ac exclusively but not a pentacene derivative.

Scheme 4. Synthesis of pentaphene 2ac.

As shown in Scheme 5, cyclotrimerization approach enables synthesis of more complex molecules from simple alkyne starting materials. Thus, cyclotrimerization of 1-alkyne 7 followed by oxidation/acid-catalyzed cyclization provided substituted triphenylenes. o-Propargyl benzyl alcohol could be synthesized by using Co-catalyzed alkyne cycloaddition reaction: The [2 + 2 + 2] cycloaddition reaction of 2,5-hexadiyne and 1,6-diyne 3a catalyzed by Dipimp/CoCl₂·6H₂O/Zn in NMP proceeded selectively to give a 7:3 mixture of adducts ii and iii and the following protodesilylation of the mixture provided 7 in 51% overall yield. Although the compounds ii and iii were inseparable, treatment of the mixture with K₂CO₃/MeOH gave 7 and unchanged iii, which could be readily separated by silica gel column chromatography. The o-propargyl benzyl alcohol 7 thus prepared was again subjected to [2 + 2 + 2] cycloaddition catalysis: Treatment of 7 with a dipimp/CoCl₂·6H₂O/Zn catalyst gave intermolecularly cyclotrimerized products 8 as a mixture of 1,3,5- and 1,2,4-regioisomers. After oxidation of the crude mixture of 8 to the corresponding tri-aldehyde 9 (37% yield from 7 through two steps), cyclization of 9 by treatment
with trifluoroacetic acid in CH$_2$Cl$_2$ proceeded smoothly trinaphthylene 10 in 87% yield. To the best of our knowledge, this is the first example of synthesis of trinaphthylenes via triple Bradsher cyclization reactions on a single benzene ring. It is noteworthy that high yield production of 10 from a regio-isomeric mixture of trisubstituted benzene 9 indicated regio-selective cyclizations of both 1,2,4- and 1,3,5-trisubstituted isomers through iv and v illustrated in Scheme 5. Thus, the compound 10 was effectively synthesized from non-aromatic substrates 6 and 3a through five steps. Trinaphthylenes are analogues of triphenylenes, which are well-known for their remarkable self-assembling and charge transporting properties, and are a simplest member of star-shaped angularly fused oligoacenes (starphene). The synthesis of these molecules is challenging.

In summary, we have demonstrated that catalytic [2 + 2 + 2] cycloaddition reactions of alkynes play an efficient role as a key reaction for construction of anthracene, pentaphene and trinaphylene structures. By taking advantage of function of annulated substructure(s) and/or further substituent(s) on anthracene such as Ph groups in 2ba, functionalization of these anthracenes might be expected. Study on utilization in this direction is underway.

Table 1 shows absorption spectral data of the new annulated anthracene derivatives, i.e., anthracenes 2aa, 2ab, 2ba, pentaphene 2ac and trinaphthylene 10, the annulated structures of which may cause a weak strain to aromatic ring(s). Comparing with data for anthracene, introduction of five-membered ring annulation onto anthracene, i.e., in 2aa and 11, did not affect UV absorption so much as observed for the known compound 12. Similarly, between 1,4-diphenyl derivatives 2ba and 13 a large difference was not observed.

In summary, we have demonstrated that catalytic [2 + 2 + 2] cycloaddition reactions of alkynes play an efficient role as a key reaction for construction of anthracene, pentaphene and trinaphylene structures. By taking advantage of function of annulated substructure(s) and/or further substituent(s) on anthracene such as Ph groups in 2ba, functionalization of these anthracenes might be expected. Study on utilization in this direction is underway.

Table 1. UV Absorption of Anthracenes 2aa, 2ab, 2ba, Pentaphene 2ac and Trinaphthylene 10.

<table>
<thead>
<tr>
<th>compound</th>
<th>$\lambda_{abs}$, nm$^a$</th>
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<tr>
<td>2aa</td>
<td>223, 260, 313, 328, 345, 362, 382</td>
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<tr>
<td>11$^b$</td>
<td>262, 310, 324, 345, 362, 382</td>
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<tr>
<td>2ab</td>
<td>233, 259, 318, 335, 353, 374, 393</td>
</tr>
<tr>
<td>2ba</td>
<td>260, 353, 372, 392</td>
</tr>
<tr>
<td>2ac</td>
<td>236, 255, 264, 296, 322, 332, 354, 364, 403</td>
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<tr>
<td>10</td>
<td>247, 259, 292, 305, 319, 343, 374, 393</td>
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<tr>
<td>anthracene</td>
<td>252, 295, 312, 326, 342, 359, 378</td>
</tr>
<tr>
<td>12$^c$</td>
<td>312, 326, 342, 359, 378$^d$</td>
</tr>
<tr>
<td>13$^d$</td>
<td>260, 320, 337, 354, 371, 391$^d$</td>
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$^a$Unless otherwise indicated, UV absorption spectra were measured for a CHCl$_3$ solution (0.1 mM). Wavelength underlined are $\lambda_{abs}$max.
$^b$See below.
$^c$In EtOH (see ref 13). For structure, see below.
$^d$In CH$_2$Cl$_2$ (see ref 14). For structure, see below.

Acknowledgments

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References and notes

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10. Diaxone 6 was prepared by the reaction of Me₂SiCCCH₂OTs with propargyl alcohol in the presence of Cul, NaI and K₂CO₃.


13. Amino acid derivatives of 1,2-dihydro-3H-cyclopenta[b]-anthracenes such as 12 have been reported: Lohier, J. F.; Wright, K.; Peggion, C.; Formaggio, F.; Toniolo, C.; Wakselman, M.; Mazaleyrat, J.-P. Tetrahedron 2006, 62, 6203.


16. ¹H NMR data of new anthracenes:

2aa: (CDCl₃, 500 MHz) δ 8.32 (s, 2H), 7.96 (dd, J = 3.5, 6 Hz, 2H), 7.80 (s, 2H), 7.42 (dd, J = 2.5, 6 Hz, 2H), 4.22 (q, J = 7.0 Hz, 4H), 3.74 (s, 4H), 1.26 (t, J = 7.0 Hz, 6H).

2ab: (CDCl₃, 500 MHz) δ 8.24 (s, 1H), 8.17 (s, 1H), 7.85 (d, J = 9 Hz, 1H), 7.57 (s, 1H), 7.16 (d, J = 2.5 Hz, 1H), 7.12 (dd, J = 2.3, 9.3 Hz, 1H), 4.22 (q, J = 7.0 Hz, 4H), 3.96 (s, 3H), 3.73 (s, 4H), 1.26 (t, J = 7.0 Hz, 6H).

2ba: (CDCl₃, 500 MHz) δ 8.27 (s, 2H), 7.84 (dd, J = 3.0, 7.0 Hz, 2H), 7.48-7.53 (m, 10H), 7.38 (dd, J = 3.0, 6.5 Hz, 2H), 5.09 (s, 4H).

2ac: (CDCl₃, 500 MHz) δ 9.09 (s, 2H), 8.14 (s, 2H), 7.93 (s, 2H), 7.80 (s, 2H), 7.57 (s, 2H), 4.23 (q, J = 7.0 Hz, 8H), 3.80 (s, 4H), 3.78 (s, 4H), 1.28 (t, J = 7.0 Hz, 12H).

10: (CDCl₃, 600 MHz) δ 8.35 (s, 6H), 7.59 (s, 6H), 4.30 (q, J = 7.2 Hz, 12H), 3.80 (s, 12H), 1.33 (t, J = 7.2 Hz, 18H).