Brønsted Acid-catalyzed Tandem Cycloaromatization of Naphthalene-based Bisacetals: Selective Synthesis of *ortho*-Fused Six-hexagon Benzenoids

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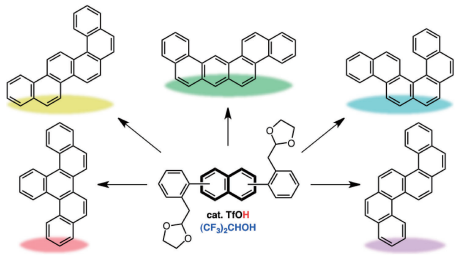

Naphthalenes bearing two acetal moieties connected by a methylene-2,1-phenylene group underwent regioselective tandem cycloaromatization using a catalytic amount of trifluoromethanesulfonic acid in 1,1,1,3,3,3-hexafluoropropan-2-ol to afford *ortho*-fused six-hexagon benzenoids with high selectivities and in excellent yields.

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Naphthalenes bearing two acetal moieties connected by a methylene-2,1-phenylene group underwent regioselective tandem cycloaromatization using a catalytic amount of trifluoromethanesulfonic acid in 1,1,1,3,3,3-hexafluoropropan-2-ol. Five substrates were successfully employed in this protocol to afford *ortho*-fused six-hexagon benzenoids with high selectivities and in excellent yields.

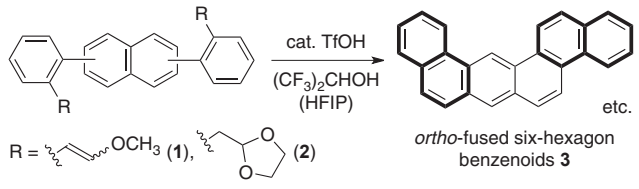
Keywords: Polycyclic aromatic hydrocarbon (PAH) | Cycloaromatization | Fluorinated alcohol

Polycyclic aromatic hydrocarbons (PAHs) have polyform structures comprising benzene rings, and are considered to be promising candidates for functional materials such as electronic devices and liquid crystals.[1] As the number of benzene rings in PAHs increases, the number of structural isomers exponentially increases. Although PAHs of substantial sizes have numerous isomers, research has typically focused on isomers of specific families such as acenes,[1b–1d,2] phenacenes,[1d,1e,3] and helicenes,[1f,4] and not on other *ortho*-fused isomers despite their great potential.[5]

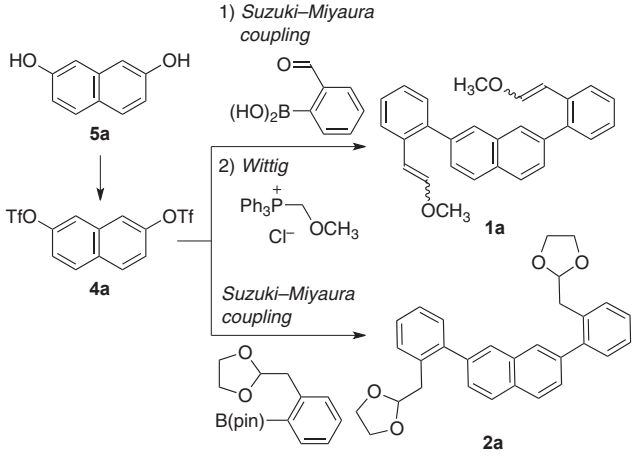
We recently developed a Brønsted acid-catalyzed cycloaromatization of carbonyl compounds, resulting in the synthesis of phenanthrene and anthracene derivatives.[6] As the method served as a powerful tool for benzene-ring construction, we embarked on the synthesis of PAHs in a variety of shapes via double cycloaromatization of substrates bearing two reactive sites.[7] This protocol would enable rapid access to higher-order PAHs by simultaneous construction of multiple fused benzene rings.

We selected naphthalenes **1** and **2** bearing two phenylacetaldehyde-related moieties as cyclization precursors (Scheme 1). Their tandem cycloaromatization afforded *ortho*-fused benzenoids, with the structure depending on the substitution pattern on the naphthalene ring. As a result, five predicted isomers of the *ortho*-fused benzenoids bearing six benzene rings were selectively synthesized in excellent yields from readily available cyclization precursors.

The cyclization precursors **1a** and **2a** bearing two phenylacetaldehyde-related moieties on the 2- and 7-positions of the naphthalene ring were readily available starting from naphthalene-2,7-diyl bis(trifluoromethanesulfonate) (**4a**), which was obtained via double *O*-sulfonylation of naphthalene-2,7-diol (**5a**) (Scheme 2). Bis(vinyl ether) **1a** was prepared via the Suzuki–Miyaura cross-coupling of **4a** with (2-formylphenyl)boronic acid, followed by a Wittig reaction with (methoxymethyl)triphenylphosphonium chloride. However, although hydrolysis of **1a** afforded the corresponding dial, it was unstable for use in the subsequent cycloaromatization. In contrast, bisacetal **2a** was directly prepared via the Suzuki–Miyaura cross-coupling of **4a** with 2-[(1,3-dioxolan-2-yl)methyl]phenylboronic acid pinacolate. Other bisacetal precursors **2b**–**2e** were also prepared similarly (see Supporting Information).



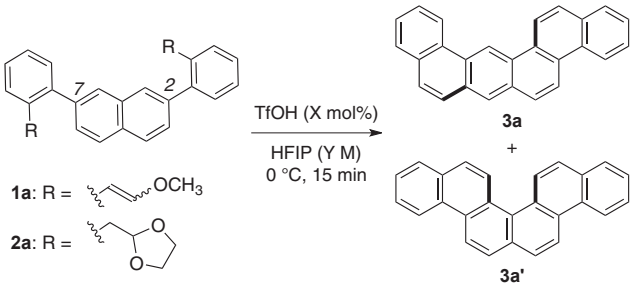
Scheme 1. Synthesis of *ortho*-fused six-hexagon benzenoids via TfOH-catalyzed tandem cycloaromatization.



Scheme 2. Preparation of bis(vinyl ether) **1a** and bisacetal **2a**.

We sought suitable conditions for tandem cycloaromatization of bis(vinyl ether) **1a**[7k,8] and bisacetal **2a**[9] as model substrates (Table 1). First, the reaction of **1a** was investigated using a catalytic amount of trifluoromethansulfonic acid (TfOH) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) as the solvent.[10] On treatment with 15 mol % of TfOH, bis(vinyl ether) **1a** at 0.05 M in HFIP underwent tandem cycloaromatization to afford dibenzo[*c*,*m*]tetraphene (**3a**)[11] and naphtho[1,2-*c*]chrysene (**3a′**) in 79% total yield and in a 75:25 ratio (Entry 1).[12] Neither more concentrated nor more dilute conditions improved the total yield of **3a** and **3a′** (Entries 2 and 3). In contrast, when bisacetal **2a** at 0.1 or 0.3 M in HFIP was treated with 15 mol % of TfOH, the product yield and ratio significantly improved to afford **3a** exclusively in almost quantitative yields (Entries 4 and 5). As a result, the efficiency and selectivity remained excellent even when the amount of TfOH was reduced to 10 mol % (Entry 7). The selective formation of **3a** is attributed to the following factors: (i) the first cycloaromatization would proceed at the α-position of the naphthalene core in accordance with the regioselectivity observed in normal electrophilic aromatic substitution

Table 1. Screening of conditions for tandem cycloaromatization of **1a** and **2a**



Entry	**1a** or **2a**	*X*/mol %	*Y*/M	Total yield/%[a]	**3a**/**3a′**[b]
1	**1a**[c]	15	0.05	79	75:25
2	**1a**[c]	15	0.03	80	75:25
3	**1a**[c]	15	0.1	71	70:30
4	**2a**	15	0.1	quant.	>99:<1
5	**2a**	15	0.3	quant.	>99:<1
6	**2a**	15	1.0	86	93:7
7	**2a**	10	0.3	quant. (97)	>99:<1
8	**2a**	3	0.3	77	>99:<1

[a]Yield was determined by ^{1}H NMR spectroscopy using CH_2Br_2 as an internal standard. Isolated yield was shown in parentheses. [b]Isomer ratio was determined by ^{1}H NMR spectroscopy. [c]*EE*/*EZ*/*ZZ* = 37:55:8.

reactions and (ii) the second cycloaromatization might proceed avoiding steric hindrance, which explains the better selectivity of bisacetal **2a**.

Not only bisacetal **2a** but also bisacetals **2b**–**2e** participated in the tandem cycloaromatization under the above-mentioned optimal conditions (Table 2). Naphthalenes **2b** and **2c**, bearing two phenylacetaldehyde acetal moieties on the 1,4- and 1,5-positions, respectively, successfully underwent tandem cycloaromatization to afford benzo[*s*]picene (**3b**)[13] and dibenzo[*c*,*l*]-chrysene (**3c**)[14] as the only products in 84% and 99% yields, respectively (Entries 2 and 3). Although the reactions of **2b** and **2c** required cycloaromatization on the less-reactive β-positions of the naphthalene core in the first cyclization, benzenoids **3b** and **3c** were obtained in high to excellent yields. Tandem cycloaromatization of 1,6- and 1,7-disubstituted naphthalenes **2d** and **2e** also proceeded to afford benzo[*a*]picene (**3d**)[11] and naphtho[2,1-*c*]chrysene (**3e**),[15] respectively, as major products (Entries 4 and 5). In each case, one of two possible products was selectively formed, presumably because regioselective cycloaromatization proceeded preferably on the α-position of the naphthalene core.

In summary, we achieved systematic synthesis of a series of rarely offered *ortho*-fused six-hexagon benzenoids via TfOH-catalyzed tandem cycloaromatization of naphthalene-based bisacetals. The use of benzenoids larger than naphthalene as platforms will enable the synthesis of more extensive *ortho*-fused benzenoids.

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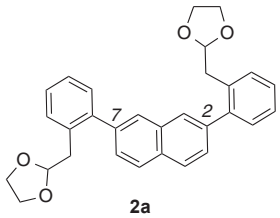
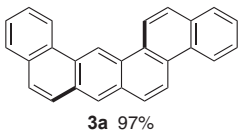
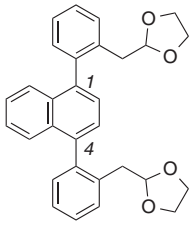
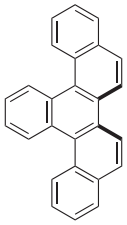
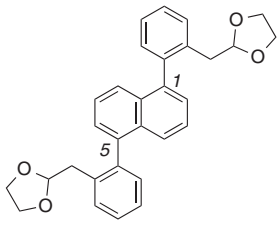
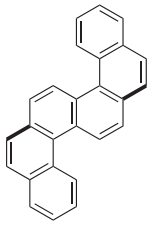
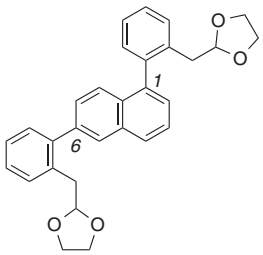
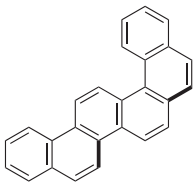
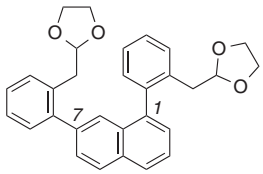
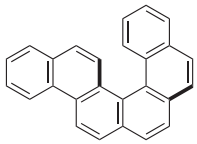
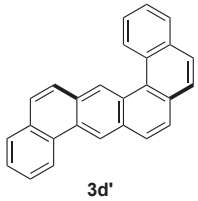
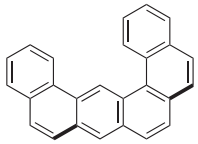
Table 2. Synthesis of *ortho*-fused six-hexagon benzenoids **3**[a]

Entry	**2**	**3**
1	 **2a**	 **3a** 97%
2	 **2b**	 **3b** 84%
3	 **2c**	 **3c** 99%
4	 **2d**	 **3d** 95% (98:2)[b]
5	 **2e**	 **3e** 87% (93:7)[b]

[a]Isolated yield. [b]Total yield of isomers. Product ratio (**3d**/**3d′** or **3e**/**3e′**) was determined by ^{1}H NMR spectroscopy.


3d'


3e'

Supporting Information is available on http://dx.doi.org/10.1246/cl.161122.

References and Notes

Dedicated to Professor Teruaki Mukaiyama in celebration of his 90th birthday (Sotsuju).

1 a) R. G. Harvey, *Polycyclic Aromatic Hydrocarbons*, Wiley-VCH, New York, **1997**. b) J. E. Anthony, *Chem. Rev.* **2006**, *106*, 5028. c) J. E. Anthony, *Angew. Chem., Int. Ed.* **2008**, *47*, 452. d) Y. Yamashita, *Sci. Technol. Adv. Mater.* **2009**, *10*, 024313. e) Y. Kubozono, X. He, S. Hamao, K. Teranishi, H. Goto, R. Eguchi, T. Kambe, S. Gohda, Y. Nishihara, *Eur. J. Inorg. Chem.* **2014**, 3806. f) M. Rickhaus, M. Mayor, M. Juríček, *Chem. Soc. Rev.* **2016**, *45*, 1542.

2 For reviews on acene synthesis, see: a) R. A. Pascal, Jr., *Chem. Rev.* **2006**, *106*, 4809. b) H. F. Bettinger, C. Tönshoff, *Chem. Rec.* **2015**, *15*, 364.

3 For selected reports on phenacene synthesis, see: a) F. B. Mallory, K. E. Butler, A. C. Evans, E. J. Brondyke, C. W. Mallory, C. Yang, A. Ellenstein, *J. Am. Chem. Soc.* **1997**, *119*, 2119. b) A.-E. Gies, M. Pfeffer, *J. Org. Chem.* **1999**, *64*, 3650. c) V. Mamane, P. Hannen, A. Fürstner, *Chem.—Eur. J.* **2004**, *10*, 4556. d) S. Some, B. Dutta, J. K. Ray, *Tetrahedron Lett.* **2006**, *47*, 1221. e) H. Okamoto, M. Yamaji, S. Gohda, Y. Kubozono, N. Komura, K. Sato, H. Sugino, K. Satake, *Org. Lett.* **2011**, *13*, 2758.

4 For reviews on helicene synthesis, see: a) A. Urbano, *Angew. Chem., Int. Ed.* **2003**, *42*, 3986. b) Y. Shen, C.-F. Chen, *Chem. Rev.* **2012**, *112*, 1463. c) M. Gingras, *Chem. Soc. Rev.* **2013**, *42*, 968.

5 For a review on a comprehensive synthesis of PAHs via photochemical oxidative cyclization, see: F. B. Mallory, C. W. Mallory, *Org. React.* **1984**, *30*, 1.

6 T. Fujita, I. Takahashi, M. Hayashi, J. Wang, K. Fuchibe, J. Ichikawa, *Eur. J. Org. Chem.* **2017**, 262.

7 For selected reports on PAH synthesis via tandem cyclization, see: a) M. B. Goldfinger, K. B. Crawford, T. M. Swager, *J. Am. Chem. Soc.* **1997**, *119*, 4578. b) M. C. Bonifacio, C. R. Robertson, J.-Y. Jung, B. T. King, *J. Org. Chem.* **2005**, *70*, 8522. c) H.-C. Shen, J.-M. Tang, H.-K. Chang, C.-W. Yang, R.-S. Liu, *J. Org. Chem.* **2005**, *70*, 10113. d) K. Kamikawa, I. Takemoto, S. Takemoto, H. Matsuzaka, *J. Org. Chem.* **2007**, *72*, 7406. e) T.-A. Chen, T.-J. Lee, M.-Y. Lin, S. M. A. Sohel, E. W.-G. Diau, S.-F. Lush, R.-S. Liu, *Chem.—Eur. J.* **2010**, *16*, 1826. f) T. Matsuda, T. Moriya, T. Goya, M. Murakami, *Chem. Lett.* **2011**, *40*, 40. g) K. Kitazawa, T. Kochi, M. Nitani, Y. Ie, Y. Aso, F. Kakiuchi, *Chem. Lett.* **2011**, *40*, 300. h) T. Nakae, R. Ohnishi, Y. Kitahata, T. Soukawa, H. Sato, S. Mori, T. Okujima, H. Uno, H. Sakaguchi, *Tetrahedron Lett.* **2012**, *53*, 1617. i) R. Umeda, S. Miyake, Y. Nishiyama, *Chem. Lett.* **2012**, *41*, 215. j) M. Little, H. Lan, J. Raftery, J. J. Morrison, J. J. W. McDouall, S. G. Yeates, P. Quayle, *Eur. J. Org. Chem.* **2013**, 6038. k) M. Murai, H. Maekawa, S. Hamao, Y. Kubozono, D. Roy, K. Takai, *Org. Lett.* **2015**, *17*, 708. l) K. Ozaki, K. Kawasumi, M. Shibata, H. Ito, K. Itami, *Nat. Commun.* **2015**, *6*, 6251. m) K. Mori, T. Murase, M. Fujita, *Angew. Chem., Int. Ed.* **2015**, *54*, 6847.

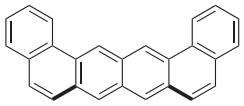
8 For cycloaromatization of vinyl ethers, see: a) R. G. Harvey, K. Lim, Q. Dai, *J. Org. Chem.* **2004**, *69*, 1372. b) R. G. Harvey, Q. Dai, C. Ran, T. M. Penning, *J. Org. Chem.* **2004**, *69*, 2024. c) K. Namba, H. Yamamoto, I. Sasaki, K. Mori, H. Imagawa, M. Nishizawa, *Org. Lett.* **2008**, *10*, 1767. d) M. Murai, N. Hosokawa, D. Roy, K. Takai, *Org. Lett.* **2014**, *16*, 4134. e) D. Roy, H. Maekawa, M. Murai, K. Takai, *Chem.—Asian J.* **2015**, *10*, 2518.

9 Cycloaromatization of acetals was reported only for acene synthesis. See: a) P. Bałczewski, M. Koprowski, A. Bodzioch, B. Marciniak, E. Różycka-Sokołowska, *J. Org. Chem.* **2006**, *71*, 2899. b) A. Bodzioch, B. Marciniak, E. Różycka-Sokołowska, J. K. Jeszka, P. Uznański, S. Kania, J. Kuliński, P. Bałczewski, *Chem.—Eur. J.* **2012**, *18*, 4866.

10 For reviews on fluorinated alcohols, see: a) J.-P. Bégué, D. Bonnet-Delpon, B. Crousse, *Synlett* **2004**, 18. b) I. A. Shuklov, N. V. Dubrovina, A. Börner, *Synthesis* **2007**, 2925. c) T. Dohi, N. Yamaoka, Y. Kita, *Tetrahedron* **2010**, *66*, 5775. d) S. Khaksar, *J. Fluorine Chem.* **2015**, *172*, 51. See also ref. 6 and references cited therein.

11 No synthetic method is known in the literatures.

12 Although dibenzo[*a*,*l*]tetracene (**3a″**) is considered to be another possible product, its formation is not detected at all under conditions we screened.



3a″

13 a) X.-Q. Tang, R. G. Harvey, *J. Org. Chem.* **1995**, *60*, 3568. b) R. G. Harvey, J.-T. Zhang, E. Luna, J. Pataki, *J. Org. Chem.* **1998**, *63*, 6405. c) D. Vasu, H. Yorimitsu, A. Osuka, *Angew. Chem., Int. Ed.* **2015**, *54*, 7162.

14 J. Brison, C. De Bakker, N. Defay, F. Geerts-Evrard, M.-J. Marchant, R. H. Martin, *Bull. Soc. Chim. Belg.* **1983**, *92*, 901.

15 Compound **3e** was synthesized as a minor product. See ref 14.