

ChemComm

Accepted Manuscript



This article can be cited before page numbers have been issued, to do this please use: M. Murai, T. Ogita and K. Takai, *Chem. Commun.*, 2019, DOI: 10.1039/C9CC00270G.



This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the [author guidelines](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the ethical guidelines, outlined in our [author and reviewer resource centre](#), still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.

Journal Name

COMMUNICATION

Regioselective Arene Homologation through Rhenium-Catalyzed Deoxygenative Aromatization of 7-Oxabicyclo[2.2.1]hepta-2,5-dienes

 Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Masahito Murai,^{a,*} Takuya Ogita,^a and Kazuhiko Takai^{a,*}

www.rsc.org/

Combined use of oxorhenium catalysts with triphenyl phosphite as an oxygen acceptor allowed efficient deoxygenative aromatization of oxabicyclic dienes. The reaction proceeded under neutral conditions and was compatible with various functional groups. Combining this deoxygenation with regioselective bromination and trapping of the generated aryne with furan resulted in benzannulative π -extension at the periphery of the PAHs. This enabled direct use of unfunctionalized PAHs for extension of π -conjugation. Iteration of the transformations increased the number of fused-benzene rings one at a time, which has the potential to alter the properties of PAHs by fine-tuning the degree of π -conjugation, shape, and edge topology.

Efficient construction of functionalized aromatic hydrocarbon skeletons is important for the syntheses of many advanced functional materials and complex natural products.¹ Because the properties of aromatic hydrocarbons depend on the degree of π -electron delocalization, controlling the size, shape, and periphery topology during synthesis is very important. Polycyclic aromatic hydrocarbons (PAHs) with an arm-chair edge have attracted attention as a novel and promising class of organic optoelectronic devices.² Compared to isostructural analogs [*n*]acenes, a greater extent of a Kekulé structure without isolated double bonds can be drawn as the resonance of this type of PAH, improving the thermodynamic stability. These structures are also commonly repeated in carbon nanotubes and nanographenes, and the development of a new benzannulative π -extension method for their basic core structure is desirable.³ In ongoing studies on the development of efficient and short syntheses of PAHs containing a fused-benzene ring in a W-shape,⁴ we envisioned a novel regioselective arene homologation approach *via* deoxygenative aromatization of 7-oxabicyclo[2.2.1]octa-2,5-dienes, which can be easily obtained by [4+2]cycloaddition of benzyne with furan derivatives (Figure 1).⁵ This method offers three major advantages:

(1) The high solubility of the nonplanar precursor, 7-oxabicyclo[2,2,1]octa-2,5-dienes, makes purification and handling of the generally insoluble PAHs derivatives easy; (2) Reaction does not require heteroatom-containing directing groups to control the regiochemistry of benzannulation (*vide infra*), and enables direct use of unfunctionalized PAHs as precursors; and (3) Iteration of the procedure allows rapid and programmed assembly of benzene rings. A major drawback for modification of PAHs is the difficulty of producing well-defined structures, which requires regioselective annulative π -extension. The current method provides a novel approach for overcoming this difficulty. While several iterative arene homologation syntheses leading to linear PAHs have been reported,⁶ this is a rare example of corresponding approaches to PAHs with an arm-chair edge.

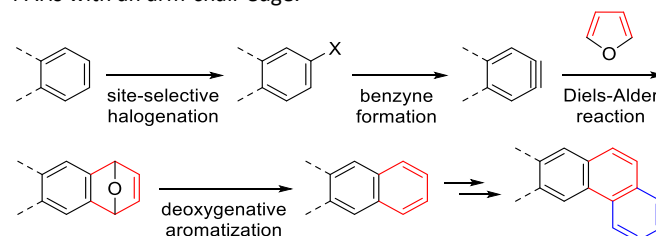


Figure 1. Hypothesis of iterative arene homologation leading to PAHs containing fused-benzene rings in a zigzag manner

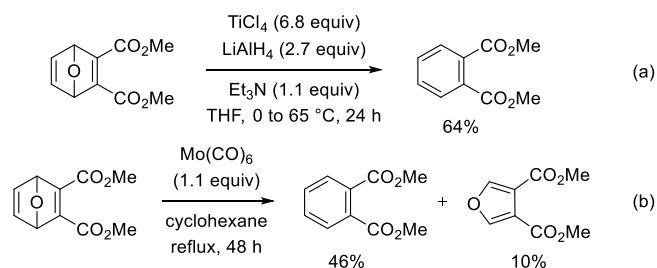
A key step for the current synthesis is the catalytic deoxygenative aromatization of 7-oxabicyclo[2.2.1]octa-2,5-dienes.⁷ Although stoichiometric amounts of low-valent titanium, iron, and tungsten reagents, which are generated *in-situ* by reduction of the corresponding metal chlorides with LiAlH_4 or BuLi , are effective for this type of deoxygenation, substrate scope as well as functional group tolerance are limited due to the high reactivity of these chemicals (Scheme 1(a)).^{7a,b,g,h} Deoxygenation with a stoichiometric amount of $\text{Mo}(\text{CO})_6$ has been also reported; however, the reaction required heating for a long period, which resulted in the formation of side products derived from *retro*-Diels-Alder reaction (Scheme 1(b)).^{7d} Note that the related dehydrative aromatization of 7-oxabicyclo[2.2.1]hepta-2-ene required strong acid promoters.⁵ Thus, development of an operationally simple and catalytic deoxygenative aromatization under essentially neutral conditions with wide substrate scope remained challenging.

Our group recently reported rhenium-catalyzed stereospecific deoxygenation of unactivated aliphatic epoxides to alkenes.^{8a} We

^a Division of Applied Chemistry, Graduate School of Natural Science and Technology, and Research Institute for Interdisciplinary Science, Okayama University, 3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan.

E-mail: masahito.murai@okayama-u.ac.jp ktakai@cc.okayama-u.ac.jp

[†] Electronic Supplementary Information (ESI) available: Experimental procedures, spectroscopic data for products, and copies of ^1H and ^{13}C NMR spectra. See DOI: 10.1039/x0xx00000x

**Scheme 1.** Previous reports of deoxygenative aromatization

also found molybdenum-catalyzed stereospecific and stereoselective deoxygenation of epoxides.^{8b} Encouraged by these successful results, other cyclic ethers were considered good candidates for deoxygenation under rhenium and molybdenum catalysis. Dimethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate **1a** was chosen as a model cyclic ether, and the deoxygenation was examined in the presence of various metal catalysts with P(OPh)₃ as an oxygen acceptor in toluene at 100 °C. The use of several rhenium catalysts produced dimethyl phthalate (**2a**) by deoxygenative aromatization (Table S1 in Supporting Information, entries 1-8).⁹ Among the catalysts screened, ReOCl₃(PPh)₂, Re₂O₇, ReCl₅, and NH₄ReO₄ gave **2a** in high yields (entries 2, 4, 5, and 6). In contrast, low-valent rhenium complexes, such as Re₂(CO)₁₀ and [ReBr(CO)₃(thf)]₂, were totally ineffective, and **1a** was recovered. Several molybdenum complexes, such as MoO₂Cl₂ and MoO₂(acac)₂, also exhibited catalytic activity, but none of them were superior to Re₂O₇ (entry 9). Because of its price and ease of handling in air, NH₄ReO₄ was used for further optimization.¹⁰ Efficiency of the reaction was strongly affected by the choice of oxygen acceptors, with the inexpensive, air-stable, and low toxicity P(OPh)₃ found to be optimal for the reaction (entries 10-15). Control experiments demonstrated that no deoxygenation by P(OPh)₃ occurred in the absence of NH₄ReO₄ even at 150 °C. In contrast to a previous study on deoxygenation of epoxides,⁸ isopropanol could be also utilized as an oxygen acceptor (entry 17). Reaction proceeded even with a reduced catalyst loading (1 mol%), although prolonged reaction time was required to achieve complete conversion of **1a** (entry 7).

The scope of substrates for the deoxygenative aromatization using NH₄ReO₄ or Re₂O₇ as catalysts is shown in Table 1.¹¹ Deoxygenation of methyl group-substituted **1b** proceeded efficiently to yield the expected phthalate **2b** in 87% yield (entry 1). The steric environment around oxygen atoms affected reaction efficiency, and deoxygenation of **1c** having two methyl groups in proximity to the oxygen atom required higher temperatures (entry 2). Fusion of the benzene ring did not reduce reaction efficiency, and naphthalene was produced from **1d** in high yield (entry 3). Functional groups, such as acyl, siloxy, bromo, and trifluoromethyl groups, were tolerated under the reaction conditions, and yielded the corresponding functionalized naphthalene derivatives **2e-2i** in good yields (entries 4-8). Although high temperatures and addition of hexamethyldisilane were required to promote deoxygenation, highly substituted oxabicyclic diene **1j** also provided the expected naphthalene **2j** in 78% yield (entry 9).¹² The current protocol was extended to catalytic deoxygenation of tricycle **1k** leading to anthracene (entry 10). Further functional group compatibility was tested briefly to find that the reaction proceeded without affecting carbonyl, alkoxy, halide, and cyano groups to furnish the corresponding phthalate **2a** in good yields (see Table S2 in SI for details).

The tolerance for a wide variety of functional groups

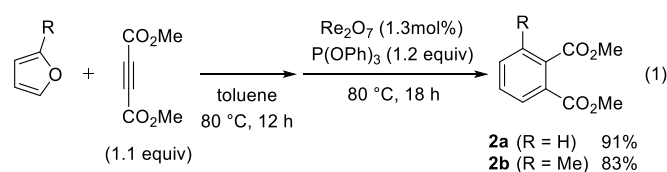
Table 1. Rhenium-catalyzed deoxygenative aromatization of **1**

| entry | substrate | temp. / °C | product | Yield |
|------------------|-----------|------------|---------|------------------------|
| 1 | | 80 | | 87% 2b |
| 2 | | 110 | | 79% 2c |
| 3 | | 80 | | 86% 2d (94%) |
| 4 ^b | | 100 | | 83% 2e |
| 5 ^b | | 100 | | 86% 2f |
| 6 | | 80 | | 91% 2g |
| 7 | | 80 | | 94% 2h |
| 8 | | 90 | | 70% 2i |
| 9 ^{b,c} | | 120 | | 78% 2j |
| 10 | | 80 | | 90% 2k |

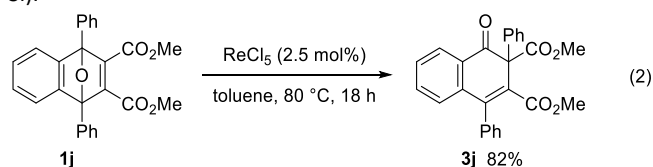
^a Isolated yields. Value in parentheses is a yield determined by ¹H NMR.

^b Re₂O₇ (1.3 mol%) was used in place of NH₄ReO₄. ^c Me₃Si-SiMe₃ (1.2 equiv) was used together with P(OPh)₃ (1.2 equiv).

demonstrated the mild conditions possible for the current deoxygenation reaction, which is an improvement over the previous protocol using stoichiometric promoters (for comparison with previous stoichiometric deoxygenation, see Table S3 in SI).⁷ Additional evidence for the mild conditions was the one-pot Diels-Alder and deoxygenation cascade leading to multisubstituted benzene derivatives (eq 1). Heating commercially available furans with dimethyl acetylenedicarboxylate in toluene, followed by addition of Re₂O₇ and P(OPh)₃ provided phthalates **2a** and **2b** in 91% and 83% yields, respectively.



The proper choice of oxygen acceptors as well as metal catalysts is important for the current deoxygenative aromatization. Especially, addition of $P(OPh)_3$ is essential not only for an oxygen acceptor but also to control the Lewis acidity of rhenium complexes. The unique switching of reactivity was observed in reaction of **1j** using $ReCl_5$ as a catalyst. Compound **3j** was obtained selectively using $ReCl_5$ in 82% yield *via* ring-opening isomerization along with a 1,2-shift of a phenyl group (eq 2),¹³ while selective formation of **2j** in 61% yield occurred by deoxygenation with the combination of $ReCl_5$ and $P(OPh)_3$ as a promoter. The structure of **3j** was determined unambiguously by X-ray crystallographic analysis (see Figure S2 in SI).



After development of a catalytic system for mild deoxygenative aromatization, regioselective arene homologation was next examined (Scheme 2). Bromination of pyrene provided 1-bromopyrene, which was converted easily to benzo[*a*]pyrene **4a** *via* Diels-Alder reaction of *in-situ* generated aryne with furan¹⁴ followed by rhenium-catalyzed deoxygenative aromatization. The latter two transformations could be performed sequentially with simple extraction of the corresponding oxabicyclic intermediate (no chromatography). Regioselectivity of overall π -extension was determined in the first bromination step, which occurred selectively at the most nucleophilic carbon atom (having the most negative Mulliken charge) of the benzene ring with the lowest aromaticity (having most positive NICS(1) values) (Figure 2). Other regioisomers were not observed, and the current protocol provided a powerful benzannulative π -extension method leading to PAHs with an arm-chair edge. Following the same three-step arene homologation procedure, chrysene underwent two-fold benzannulation at the convex armchair edge (K-region) leading to dibenzo[*g,p*]chrysene **4b**. Diels-Alder reaction of bisaryne generated from 6,12-dibromochrysene with furan gave oxabicycles as a mixture of two stereoisomers in this case, and the following rhenium-catalyzed deoxygenation proceeded equally well with both isomers. Sequential regioselective benzyne generation from 3-bromophenyl(mesityl)iodonium salt prepared from 3-bromophenylboronic acid¹⁵ and interception with two different furans produced unsymmetrically substituted phenanthrene **4c**. In this case, the first reaction with furan gave the mono-oxabicyclic having a bromide group, which served as a second benzyne generator. Selective annulative π -extension of dibenzofuran gave naphtho[1,2-*b*]benzofuran **4d**, in which the regioselectivity was determined in the first chelation-controlled lithiation at the 4-position of dibenzofuran.

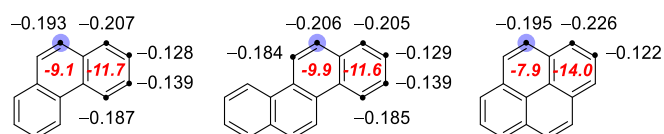
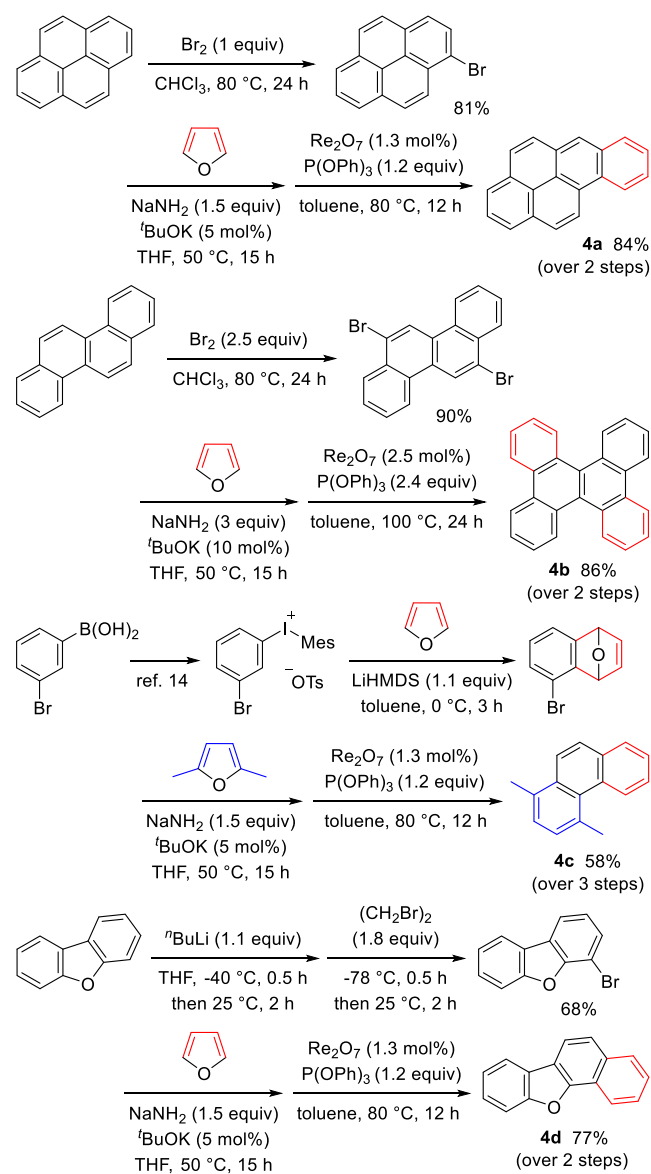


Figure 2. Rationalization of regioselectivity of the first electrophilic bromination step. Mulliken charge density obtained by DFT calculation (B3LYP functional with the 6-31G(d) basis set in the Gaussian 09 program) are shown as black numbers and the experimentally brominated sites are indicated by blue circles. NICS(1) values at the center points of each ring were calculated at

the GIAO-B3LYP/6-31G(d) level of theory and are represented as red numbers.

DOI: 10.1039/C9CC00270G



Scheme 2. Regioselective arene homologation (see SI for reaction condition details)

Finally, iterative arene homologation was conducted (Scheme 3). Starting from benzene, gold-catalyzed bromination provided bromobenzene,¹⁶ which was converted easily to naphthalene **2d** *via* Diels-Alder reaction of benzyne with furan followed by rhenium-catalyzed deoxygenative aromatization. Repeating these three transformations provided phenanthrene **4e**, which then underwent further regioselective benzannulation to furnish triphenylene **4f**. The method increased the number of fused-benzene rings regioselectively one at a time, which has the potential as a bottom-up approach to alter the properties of PAHs by fine-tuning the degree of π -conjugation, shape, and edge topology.¹⁷

In conclusion, catalytic deoxygenative aromatization of oxabicyclic dienes under mild conditions was achieved. In combination with regioselective bromination and *in situ*

