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

Received 00th January 20xx, Accepted 00th January 20xx DOI: 10.1039/x0xx00000x

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Published on 01 February 2019. Downloaded by Webster University on 2/1/2019 9:15:09 AM

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 topologyduring 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 synthesies 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 benzynes with furan derivatives (Figure 1).⁵ This method offers three major advantages: (1) The high solubility of the nonplanar precursor, 7oxabicyclo[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. Although stoichiometric amounts of low-valent titanium, iron, and tungsten reagents, which are generated in-situ by reduction of the corresponding metal chlorides with LiAlH₄ 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 $Mo(CO)_6$ 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 7oxabicyclo[2.2.1]hept-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

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

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Scheme 1. Previous reports of deoxygenative aromatization

found molybdenum-catalyzed stereospecific also and stereoselective deoxygenation of epoxides.^{8b} Encouraged by these successful results, other cyclic ethers were considered good candidates for deoxygenation under rhenium and molybdenum 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-Dimethyl catalysis. 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(PPh₃)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 MoO_2Cl_2 and $MoO_2(acac)_2$, 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



^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 Re_2O_7 and $P(OPh)_3$ provided phthalates **2a** and **2b** in 91% and 83% yields, respectively.

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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 ReCl₅ as a catalyst. Compound **3j** was obtained selectively using ReCl₅ 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 ReCl₅ 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 1bromopyrene, 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 armchair edge. Following the same three-step arene homologation procedure, chrysene underwent two-fold benzannulation at the convex armchair edge (K-region) leading to dibenzo[q,p]chrysene 4b. Diels-Alder reaction of bisaryne generated from 6,12dibromochrysene 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 3prepared bromophenyl(mesityl)iodonium salt from 3bromophenylboronic acid¹⁵ and interception with two different furans produced unsymmetrically substituted phenanthrene ${\bf 4c}.$ In this case, the first reaction with furan gave the mono-oxabicycle 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 4position 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

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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

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Scheme 3. Regioselective iterative arene homologation of benzene

trapping of the generated aryne with furan, the reaction provided various PAHs with an arm-chair edge. Iterative use of these transformations allowed the rapid and programmed arene homologation at the periphery of the PAHs. This fine-tuning of the π -conjugated structure is particularly important for providing insights into the structure-property relation for production of high-performance functional materials.

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