Mechanochemical Synthesis of Extended Iptycenes

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S *Supporting Information*

ABSTRACT: Iptycenes are intriguing compounds receiving considerable attention as a result of their rigid noncompliant three-dimensional architecture. The preparation of larger iptycenes is often problematic, as a result of their limited solubility and synthetic procedures involving multiple Diels−Alder reactions under harsh extended reaction conditions. We report a mechanochemical synthesis of structurally well-defined iptycenes through an iterative reaction sequence, wherein Diels−Alder reactions and a subsequent aromatization afford higher order iptycenes. We further report that double Diels−Alder reactions under solvent-free condition provide facile access to highly functionalized iptycenes with molecular weights over 2000 Da. Quartz crystal microbalance measurements reveal that these materials efficiently absorb the aromatic hydrocarbons benzene and toluene.

Three-dimensional rigid molecular structures have found increasing applications in the design of advanced functional materials.[1] Among various molecular architectures, iptycenes that have arene bridges in extended [2.2.2] bicyclic ring systems[2] have been widely used in supramolecular chemistry and materials science.[3] These utilities rely on their unique geometrical characteristics and the ability to incorporate a variety of functional groups.[4] Specific applications include the ability of iptycene groups to prevent cofacial packing in the solid state and thereby produce highly emissive semiconductive polymer films.[5] The resulting films have molecularly enforced porosity that facilities molecular and gas diffusion for the creation of sensory[5] and gas separation materials.[6] Extended iptycenes generally are more effective at creating additional degrees of free volume.[7] Herein, we report an iterative reaction sequence to prepare extended iptycenes, wherein a Diels−Alder reaction and a subsequent aromatization afford large iptycenes. Critical to the success of this approach are the use of mechanochemical activation and the identification of suitable additives that efficiently promote the reactions under solvent-free conditions. We demonstrate rapid access to functionalized iptycenes with molecular weights over 2000 Da.

Similar to the original synthesis of triptycene,[8] we utilize a Diels−Alder reaction to create the [2.2.2] bicyclic ring system. To achieve large, soluble and structurally well-defined iptycenes, we employ a strategy for incorporation of an aromatization with functional group incorporation after each Diels−Alder reaction. Iterative cycling of this process provides rapid access to functionalized extended iptycenes. The functional groups can be used to modify the resultant properties such as solubility. 1,4-Anthraquinone is an ideal

building block for this scheme, and its reaction with anthracene produces an enolizable 1,4-diketone that regenerates an anthracene derivative for the subsequent Diels−Alder reactions (Scheme 1).

Scheme 1. Designed Reaction Sequence for the Synthesis of Higher Order Iptycenes
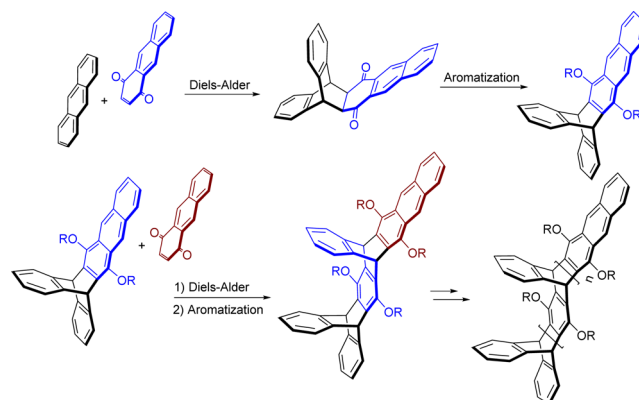

There are two challenges to achieve the above-mentioned synthetic sequence. First, thermally activated Diels−Alder reactions often require long reaction times, which makes iterative synthetic routes impractical.[9] This limitation cannot be solved using higher temperatures, because retro-Diels−Alder reactions, which are entropically favored, will give rise to lower yields. Although strong Lewis acids, such as aluminum chloride (AlCl$_3$), are known to promote Diels−Alder reactions, these catalysts are not compatible with many functional groups.[10] Second, anthracene-1,4-diol (**2**) produced by the enolization of **1** undergoes rapid air oxidation to form anthracene-1,4-dione (**3**) (Scheme 2a). As a result, a synthesis with a coupled functionalization−aromatization step, as illustrated in Scheme 1, is preferred. Alternative routes avoiding oxidation include a silicon protection and deprotective sulfonylation sequence, which suffers from a limited yield (Scheme 2b).[11] We envisioned to address both challenges by using mechanochemical synthesis.[12] Additionally, the high concentration and solvent-free conditions are compatible with sensitive intermediates that have greater persistence in the solid state.[13]

Mechanochemical activation has been previously used to promote Diels−Alder reactions. Cyclopentadiene and maleic anhydride were reported to undergo efficient cycloaddition reaction under mechanochemical milling conditions.[14a] In

Scheme 2. Oxidation (a) and Low Functionalization Yields (b) Represent Challenges in Iptycene Synthesis in Solution[11]
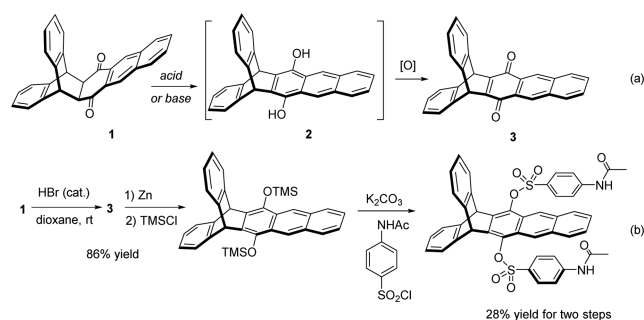
addition, 2-naphthol has been used as an additive to promote the Diels−Alder reaction between *p*-benzoquinone and electron-rich 9,10-dimethylanthrancene.[14b] However, anthracene itself was found to be relatively unreactive under the reported conditions.[14b] We began our investigation by screening various mild Lewis acids with the aim to lower the LOMO energy of 1,4-anthraquinone via coordination of the carbonyl groups. It was quickly found that anhydrous ZnCl$_2$ was a suitable additive for the Diels−Alder reaction. A 5:1:1 ratio of ZnCl$_2$:anthracene:1,4-anthraquinone gave full conversion under a vibration frequency of 30 Hz at room temperature in 4.5 h. Column chromatography is not required to purify the product. The crude product is simply dissolved in dichloromethane and washed with 3 N HCl to remove ZnCl$_2$. After concentration, pure **1** is isolated in 87% yield by simple precipitation from methanol (Scheme 3a). To our surprise,

Scheme 3. Optimized Reaction Condition for Each Step of the Iterative Reaction Sequence[a]
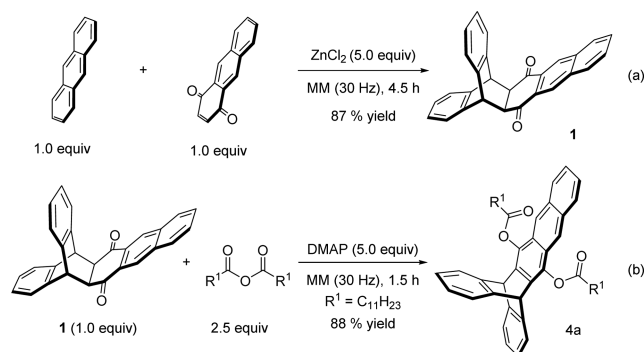
[a]MM stands for mechanical milling.

EtAlCl$_2$, a much stronger Lewis acid than ZnCl$_2$ was ineffective in promoting the current Diels−Alder in dichloromethane at room temperature. Moreover, the conversion is lower than 5% if the reaction was carried out in 1,2-dichloromethane in the presence of ZnCl$_2$ at 80 °C after 24 h. These results clearly indicate the mechanical activation has a dramatic influence on the rate of Diels−Alder reaction and allows the reaction to proceed under milder reaction conditions.

Encouraged by the production of **1**, we set out to develop conditions for the aromatization/functionalization step under ball-milling conditions using lauric anhydride as an acylating reagent and cesium carbonate as the base. It is noteworthy that the use of acid chlorides afforded lower yields as a result of reactions with the base. Moreover, oxidation is problematic

under these conditions and quinone **3** (Scheme 2) is a major byproduct. We envisioned that this problem could be addressed by using base *N,N*-dimethylpyridine (DMAP) as both a base and an activating agent for the lauric anhydride. As a result of the acceleration of the acylation, the undesired oxidative pathway was completely suppressed and **3** is not observed. The crude product is dissolved in dichloromethane and filtered through a short pad of silica gel. After concentration, the pure product **4a** is isolated in 88% yield by precipitation from methanol (Scheme 3a). We find that benzoic anhydride, triphenyl silyl chloride, and tosyl chloride are also suitable electrophiles under the condition described in Scheme 3b, thereby giving access to a series of anthracene derivatives appended with various functional groups **4b−d** (Figure 1).
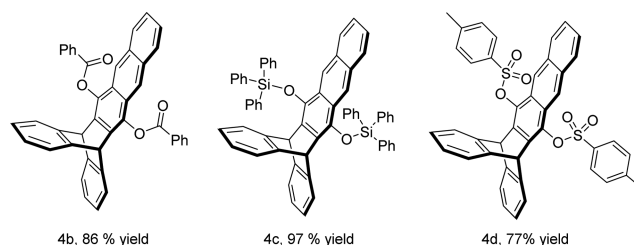

Figure 1. Diversified anthracene derivatives prepared under mechanochemical conditions.

To achieve extended iptycenes by using the iterative reaction sequence illustrated in Scheme 1, we examined Diels−Alder reactions between **4a−d** and 1,4-anthraquinone. The anthracene derivative **4a** with alkyl ester functional groups gave a low yield of Diels−Alder product in the presence of ZnCl$_2$, and no Diels−Alder product was observed with **4b**, **4c**, and **4d**, probably as a result of steric hindrance introduced by the bulky substituents. Steric effects and reduced diffusion rates can present significant difficulties under solvent-free conditions. It is also possible that competitive interaction of the ZnCl$_2$ with the ester can reduce the activation of 1,4-anthraquinone. We attempted the liquid-assisted grinding (LAG) method to increase the mobility of the reactants by adding varying amounts of chloroform (5−100 μL); however, only low conversions (<15%) were observed, which indicates that a higher acidity may be required to promote the current reaction.[15] To provide extra activation of the dienophile, we employed a Brønsted acid additive. It is known that a Lewis acid and a Brønsted acid are symbiotic with higher acidity and catalytic enhancements that are larger than an additive effect of individual effects.[16] After a series of screening experiments, we found that the addition of perfluorononanoic acid (C$_8$F$_{17}$COOH) allowed the desired transformation to proceed with high efficiency (Scheme 4a). Although Diels−Alder product **5** could be obtained in solution using AlCl$_3$ as the Lewis acid, both the yield (66% vs 89%) and stereoselectivity (exo/endo, 56:44 vs 86:14) are lower than that obtained under ball-milling conditions (see Figure S2 in SI for details). Furthermore, the attempt to prepare Diels−Alder product **7** in solution using AlCl$_3$ was unsuccessful and **6** decomposed under the experimental condition. Repeating the designed iterative reaction sequence successfully produced the extended iptycene in good yield (Scheme 4b). As a result of the incorporated alkyl groups, all the iptycenes synthesized through this method are highly soluble in common organic solvents, such as dichloromethane, chloroform, and tetrahydrofuran. The products can

Scheme 4. Iterative Reaction Sequence for the Synthesis of an Extended Iptycene[a]
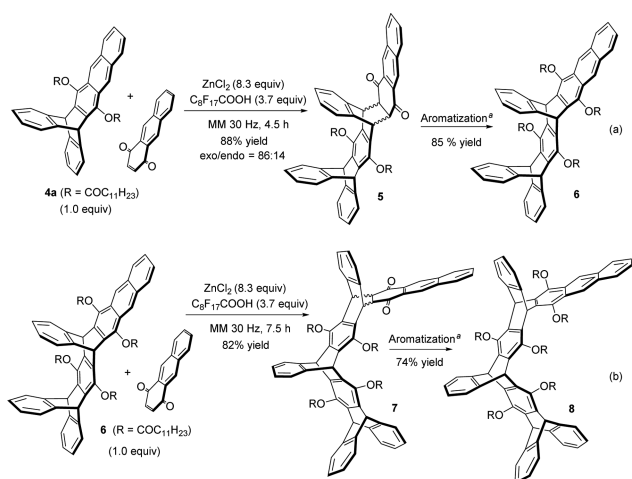
[a]The same conditions as described in Scheme 3b.

be purified by precipitating the crude product from methanol as described in isolation of **4a**.

To accelerate the preparation of larger iptycenes, we examined the feasibility of a double Diels–Alder reaction by using triptycene diquinone[17] as a bifunctional dienophile. By slightly increasing the amount of ZnCl$_2$ and the additive C$_8$F$_{17}$COOH, the desired double Diels–Alder product was obtained in satisfactory yield (Scheme 5), demonstrating the

Scheme 5. Synthesis of High Ordered Iptycene through a Double Diels–Alder Reaction
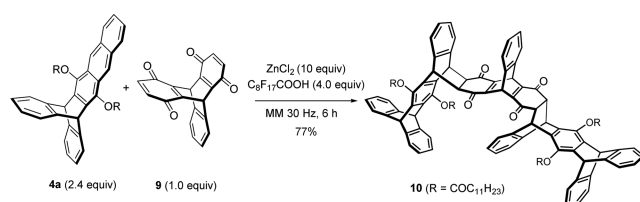
high efficiency of the mechanochemical reaction. Interestingly, although multiple stereoisomers can be generated, only one isomer (the stereochemistry is determined based on NOESY experiments and a detailed assignment of ^{1}H NMR signals is included in Figure S3 in SI) was obtained in this reaction as shown in Scheme 5. With the double Diels–Alder product **10** in hand, an iptycene-based molecular cage (the cavity is highlighted in blue in Scheme 6) appended by various groups can be easily constructed through a 4-fold esterification.

Scheme 6. Synthesis of Molecular Cage Based on High Order Iptycene
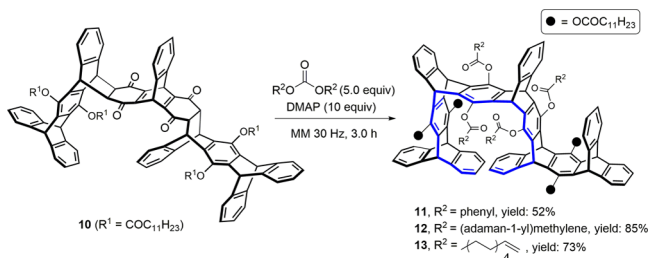
Considering the noncompliant three-dimensional rigid structure of iptycenes **10−13**, we postulated these materials to have good gas absorption properties. Furthermore, we hypothesize that the molecular cage structure generated by the concave structure of iptycene may provide selectivity toward specific guest molecules. The absorption properties of **10−13** for selected molecules were tested by using a quartz crystal microbalance (QCM), and the results are summarized in Figure 2. These molecules were found to absorb organic vapors readily
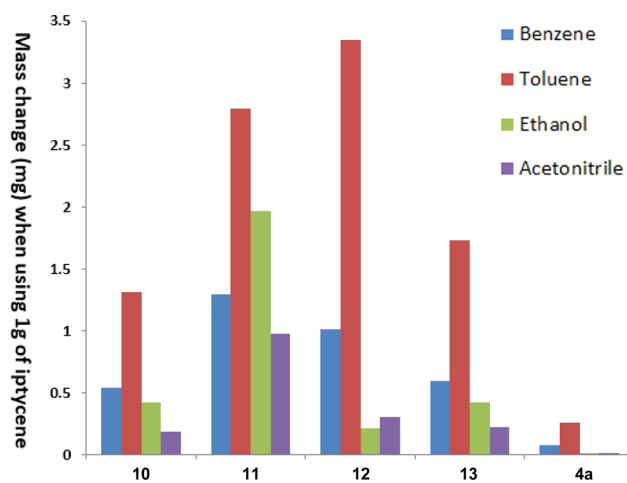

Figure 2. Gas absorption ability of **10−13**, and **4a** determined by quartz crystal microbalance.

at low concentrations (500 ppm). Despite the fact that hydrogen bonding and dipole interactions are strengthened in solid state structures, **10**, **12**, and **13** showed clear selectivity for the absorption of aromatic molecules over ethanol and acetonitrile. This latter effect can also be considered to be in part a result of the hydrophobic nature of these materials and the prospects for C−H−π interactions. Interestingly, the gas absorption selectivity can be tuned by incorporation of different side groups. For instance, **11** with a high arene composition showed a better uptake of all four kinds of gas vapor as compared to **10**, whereas **12** containing adamantyl groups displayed significantly enhanced selectivity toward benzene and toluene over ethanol and acetonitrile (Figure 2). It is noteworthy that **4a** bearing an anthracene unit shows a much lower absorption of benzene and toluene compared to **10−13** (Figure 2), which indicates that the noncompliant structure is important and the absorption is more likely to occur in the cavities within the materials than on the surface. We expect these materials can be used as filters media or preconcentrators to remove selectively or detect organic vapors.

In summary, we have developed an efficient method for the preparation of extended iptycenes by using an iterative reaction sequence. By identifying proper additives, all the synthetic steps are achieved by using mechanochemical activation under solvent-free conditions. The current modular approach allows for access of large iptycenes bearing various sides groups that are difficult to synthesize by traditional methods. It is also demonstrated that mechanochemical reaction is amenable to prepare complex molecules through a multistep synthesis.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b09011.

> Experimental procedures and characterization data for all new compounds (PDF)

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Notes

The authors declare the following competing financial interest(s): A patent has been filed on these methods.

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