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KHMDS mediated synthesis of 9-arylfluorenes from dibenzothiophene dioxides and arylacetonitriles by tandem S_NAr-decyanationbased arylation[†]

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A straightforward KHMDS mediated synthetic route to 9-arylfluorenes from readily available starting materials has been developed. This reaction involves S_NAr reactions of dioxide with arylacetonitriles, followed by decyanation reaction. The proposed transformation can also be used to furnish a densely arylated indene.

9-Arylfluorenes are important structural frameworks that find application in diverse fields.¹ More specifically, because of their unique electronic and photonic properties,² these compounds are widely used in materials science,³ *i.e.*, in organic electronics,⁴ blue fluorescent organic light-emitting materials,⁵ semiconductors,⁶ photovoltaic cells,⁷ etc. The C-H bond at the 9-position of 9-arylfluorenes is acidic and hence can serve as a ligand in organometallic chemistry.8 Much research has been undertaken to prepare 9-arylfluorene derivatives in the last few years. Pre-functionalized 9-bromofluorene was found to react with phenylboronic acid in the presence of organostannoxanesupported palladium nanoparticles as the catalyst to afford the corresponding 9-arylfluorenes.9 Hao and co-workers reported a zinc-mediated coupling of 9-bromofluorene with arenes to obtain 9-arylfluorenes.¹⁰ An alternative and straightforward method in this regard is the palladium-catalyzed direct C-H bond arylation of fluorene with aryl halides.¹¹ A combination of bimetallic Pd-Sn and AgPF₆ is reported to catalyze the intramolecular tandem reaction of 2-arylbenzaldehyde with electron-rich arenes to give the desired 9-arylfluorenes.¹² However, most of the reported methods require transition-metal catalysts or specially designed precursors that are obtained via multiple synthetic steps. Furthermore, these strategies are efficient, but the residual transition metals in the final pro-

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† Electronic supplementary information (ESI) available: Experimental procedure, spectra. CCDC 1866811. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c80b02355g ducts would adversely affect the performance of the device in which they are used. Moreover, the commercial non-availability of the catalysts and limited reaction scope hinder the practical utility of the aforementioned methods.

On the other hand, there are very few reports on the transition-metal-free synthesis of 9-arylfluorene derivatives. In one such example, *i.e.*, the reduction of 9-aryl-9-fluorenol with an $Et_3SiH/Et_2O\cdot BF_3$ system, the precursor carbinol was prepared by the reaction of 9-fluorenone with aryllithium or an aryl Grignard reagent *via* a two-pot approach (method-I, Fig. 1).¹³ A Lewis acid or Brønsted acid could be used to catalyze the intramolecular Friedel–Crafts cyclization of an *ortho*-biaryl alcohol/ acetate (method-II).¹⁴

In general, substituted biaryls provide regio-isomeric mixtures in Friedel–Crafts cyclization.^{14a} In 2014, Zhang and Zheng *et al.* developed a TfOH-catalyzed tandem ring-closing



Fig. 1 Recent strategies for transition-metal-free synthesis of 9-arylfluorenes.

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reaction of 2-arylbenzaldehydes with electron-rich arenes (method-III).¹⁵ Ping Liu and Yan Liu groups jointly developed an efficient method based on the reductive coupling of N-tosylhydrazones with arylboronic acids, a two-step reaction in which the reactants were added sequentially (method-IV).¹⁶ In spite of these elegant methods, there still remain need to develop novel strategies to synthesize 9-arylfluorene under transition-metal free conditions. Recently, Yorimitsu's group reported a very interesting reaction, the aromatic metamorphosis of dibenzothiophenes into a different ring system. This method is valuable as it allows for the cleavage of aromatic rings, which are typically considered uncleavable.¹⁷ In particular, the twofold S_NAr reaction of dibenzothiophene dioxide is considered a sustainable strategy for aromatic metamorphosis, since it does not require transition-metal catalysts. Dibenzothiophene dioxide can be transformed into dibenzophosphole oxide,¹⁸ spirocyclic 9,9-diarylfluorenes,¹⁹ and carbazoles²⁰ by reaction with phenylphosphine, cyclic diarylmethanes, and aniline nucleophiles, respectively. The key to the success of this twofold S_NAr reaction is the choice of a suitable nucleophile, such as a species with reasonably acidic geminal protons. With these concepts in mind, we envisioned that benzyl cyanide²¹ would be a promising coupling partner for dibenzothiophene dioxide in twofold S_NAr reactions to access 9-phenyl-9H-fluorene-9-carbonitrile (7).

We commenced our study using reaction conditions similar to those established for carbazole synthesis (Table 1, entry 1).²⁰ To our delight, we could isolate a highly nonpolar product by the treatment of dibenzo[b,d]thiophene 5,5-dioxide (1a) with benzylcyanide (2a; 2 equiv.) in the presence of KN

base

solvent

Table 1 Optimization of reaction condition^a



^{*a*} Reactions were carried out using **1a** (0.5 mmol), **2a** (1.5 mmol), base (1.5 mmol), solvent (1 mL) at 100 °C for 24 h. ^{*b*} KN(SiMe₃)₂ and LiN (SiMe₃)₂ were 0.5 and 1.0 M solutions in toluene, respectively. ^{*c*} Isolated yield. ^{*d*} Performed with **2a** (1.0 mmol) at 80 °C for 16 h. ^{*e*} NR: No reaction.

(SiMe₃)₂ (potassium hexamethyldisilazide; KHMDS, 3 equiv.) at 80 °C in dioxane for 16 h. After careful analysis of the NMR spectra, we concluded that the abovementioned product was 9-phenylfluorene (3a). Compound 3a was probably formed by the S_NAr reactions of 2a with 1a, followed by a decyanation reaction. This result prompted us to identify the optimal reaction conditions for the formation of 3a. When using 2 equiv. of the starting material 2a, the reaction did not proceed to completion even at 80 °C. Hence, we decided to perform the optimization studies using 3 equiv. of 2a at 100 °C for 24 h in various solvents. The yield of the product 3a was 69% using dioxane as a solvent (entry 2). Other nonpolar solvents such as toluene yielded poor amount of 3a (entry 3). The reaction with other ethereal solvents such as THF and 1,2-dimethoxyethane (DME) gave the desired product 3a in moderate yield (entries 4 and 5). Highly polar DMSO did not found to be good solvent (entry 6). Use of nonpolar solvent petroleum ether gave the corresponding product in 81% yield (entry 7). Finally, the effect of bases was examined (entries 8-13). Other alkaline metal salts of hexamethyl disilazane such as $Li(NSiMe_3)_2$ (1.0 M in toluene) and $Na(NSiMe_3)_2$ was inferior (entries 8 and 9). The reaction with Cs₂CO₃ K₂CO₃, and K₃PO₄ resulted with no conversion (entries 10-12). The strong base KOH was not effective (entry 13).²² These results suggest that 3 equiv. of 2a, 3 equiv. of K(NSiMe₃)₂ base in toluene/pet.ether at 100 °C for 24 h would be a better reaction condition for S_NAr-decyanation based arylation process. With the optimized reaction condition in hand, we next involved in exploring the scope of the reaction.

At first, reaction between **1a** and various arylacetonitrile **2** were investigated under the optimized reaction condition (Table 2).

The electron neutral phenyl substituted acetonitrile 2a reacted with 1a to give the corresponding product 3a in 81% yield. 9-([1,1'-Biphenyl]-4-yl)-9H-fluorene (3b) was isolated in albeit in moderate yield. Electron donating substituents such as methyl and methoxy on para-position of phenyl ring furnished the corresponding products 3c and 3d in 93% and 52% yields, respectively. Notably, typical hydroxyl protecting groups such as methoxymethyl and benzyl moieties in 3e and 3f survived under the basic reaction conditions. The N-heterocycle pyrazole bearing arylacetonitrile 2g was tolerated under the reaction condition to give 3g in 62% yield. The presence of α-acidic protons on pyrazole ring might be responsible for obtaining moderate yield. Synthetically viable halo groups survived under the reaction condition. The reaction of 2-(4-chlorophenyl)acetonitrile (2h) and 2-(4-fluorophenyl)acetonitrile (2i) with 1a were conducted independently and the corresponding products 3h and 3i were isolated in 78% and 57% yields, respectively. The meta-substituted 9-(m-tolyl)-9H-fluorene (3j) was obtained in excellent yield. Despite its steric hindrance, 2-(2-methoxyphenyl)acetonitrile (2k) participated in the reaction to give 3k in reasonable yield.

Next, we examined the scope of dibenzothiophene dioxide, and the results are shown in Table 3. In general, Friedel–Crafts cyclization reactions may deliver mixture of regio-isomeric pro-

 Table 2
 Substrate scope of aryl acetonitriles^{a,b}



^{*a*} Reactions were carried out using **1a** (0.5 mmol). ^{*b*} Isolated yields.

ducts (method-II and III, Fig. 1). It is worthy to note that the transformations with substituted dibenzothiophene dioxides are immanent regio-specific. For instance, the initial substitution pattern on dibenzothiophene dioxides were retained in the final products **4b–e**. π -Extended 9-arylfluorenes such as 3,9-diphenyl-9*H*-fluorene (**4b**) and 3,6,9-triphenyl-9*H*-fluorene (**4c**) were isolated in 69% and 76% yields, respectively. Similarly, 2-pyrazolyl substituted sulfone **1d** smoothly underwent reaction with **2a** to furnish **4d** as a sole product in albeit moderate yield. Other regio-isomeric sulfone such as 3-phenyl-dibenzothiophene 5,5-dioxide (**1e**) participated in the reaction to give **4e** in 53% yield.

Encouraged by the good performance of the S_N Ar-decyanation-based arylation strategy, we next investigated the effect of 2,3-diphenylbenzothiophene 1,1-dioxide (5). Eventually, the

 Table 3
 Substrate scope of dibenzothiophene dioxide^{a,b}



^a Reactions were carried out using **1a** (0.5 mmol). ^b Isolated yields.



Scheme 1 Synthesis of 1,2,3-triphenyl-1H-indene.

densely arylated 1,2,3-triphenyl-1*H*-indene (6) was obtained from simple starting materials, albeit in moderate yield (Scheme 1).

To identify the mechanism underlying the S_NAr -decyanation based arylation, the following experiments were conducted (Scheme 2).

We initially envisioned that the transformation proceeds *via* a two-fold S_NAr reaction to give 7, which then undergoes reductive decyanation in the presence of $K(NSiMe_3)_2$.²³ After performing a few control experiments, we were able to isolate 7 by reducing the amounts of the base and 2a, in a shorter time.

The structure of 7 was unambiguously confirmed by X-ray analysis (see ESI[†]). Subsequent exposure of 7 to $K(NSiMe_3)_2$ at 100 °C for 12 h did not afford **3a**, and the starting material was



Scheme 2 Elucidation of mechanism.



Scheme 3 Deuterium scrambling experiment.

partially decomposed. The mechanism for departure of cyanide from 7 is unclear.²⁴ The plausible mechanism for this transformation would be an intermolecular S_NAr reaction of arylcyanide 2 with 1a in the presence of K(NSiMe₃)₂ provides the corresponding ring opening product. Trimethylsilylation of SO₂K unit with HN-(SiMe₃)₂, generated *in situ*, delivers 8.^{20,25} Deprotonation of active methyne proton in compound 8 followed by intramolecular S_NAr reaction would take place to afford 7. The elimination of cyanide group from 7 would provide 9-arylfluorene 3.

The acidic nature of the hydrogen at the 9-position of **3a** was confirmed by a deuterium scrambling experiment, which revealed the formation of a stable Hückel aromatic compound 9-arylfluorenyl anion²⁶ in the presence of $KN(SiMe_3)_2$ (Scheme 3).

In summary, we have demonstrated a KHMDS mediated synthesis of 9-arylfluorenes from readily available starting materials arylacetonitrile and dibenzothiophene dioxide.

The initial substitution pattern of the dibenzothiophene derivatives was retained in the final 9-arylfluorenes. This method could also be extended to the preparation of the densely arylated 1,2,3-triphenyl-1*H*-indene. Current efforts are directed at investigating the mechanism and application of the final products in materials chemistry.

Conflicts of interest

There are no conflicts to declare.

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