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COMMUNICATION

Aryl Radicals Induced Desulfonylative *ipso*-Substitution of Diaryliodonium Salts: An Efficient Route to Steric Hindered Biarylamines

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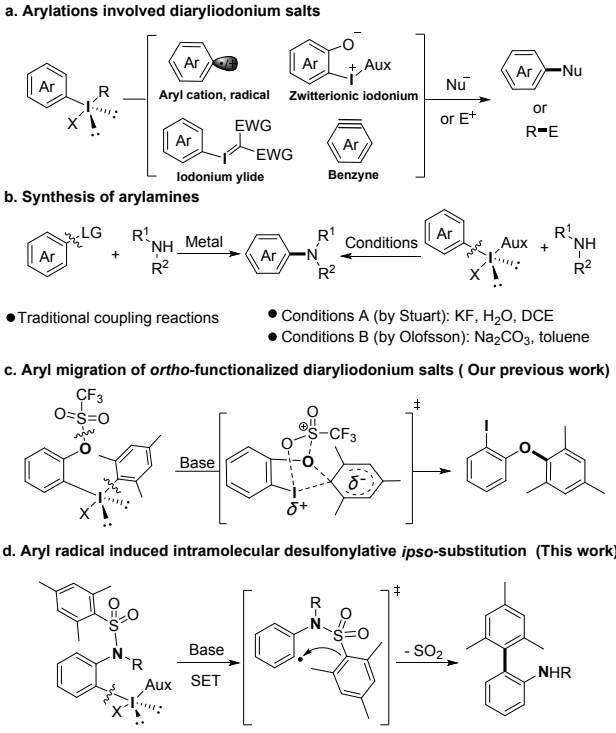
By using vicinal arylsulfonamide substituted diaryliodonium salts, a cascade of desulfonylation/aryl migration was promoted by triethylamine in synthesis of steric hindered biarylamines, which operated in a radical induced reaction pathway. The products were readily converted into a variety of important synthons. Furthermore, double coupling reactions in one pot with the product of *N*-methyl biarylamine provided a potentially attractive molecule in OLEDs.

The chemistry of diaryliodonium salts has been a topical subject of growing research interest.[1] Their unique reactivity as highly electrophilic precursors caused by the hyper nucleofuge of the aryliodo moiety, enables to operate a variety of aromatic transfer reactions.[2] For the mechanistic discussion of iodonium salts involved tranformations, the conclusive insight on reactive intermediates generally included aryl cation, aryl cation radical, iodonium ylide, zwitterionic iodonium or benzyne (Scheme 1, a).[3] The mechanism proposals were explained by the employed substrates and reaction conditions, which were often closely balanced and in competition with each other by collection of the products.[4] Gaunt and coworkers have proposed aryl cation species in the copper catalyzed arylations of arenes, alkenes and enamines.[5] In particular, the use of diaryliodonium salts provides an access to aryl radicals. Formally, previous studies on cationic polymerization have revealed free iodoarene radicals as the key photoinitiator under photolysis.[6] Related to synthetic methodology, Kita and coworkers pioneered the oxidative coupling reactions by a single-electron-transfer process, in which the charge-transfer complex of hypervalent iodine atom and aromatics generated cation radicals with the aid of TMSOTf in hexafluoroisopropanol.[7] Three reports from the research groups of Zhang and Yu, Tobisu and Chatani, Wang and Ding, described diaryliodonium salts as aryl radical sources in arylations of arenes, heteroarenes and quinones under basic conditions or visible light-mediated photoredox catalysis.[8] Very recently, Lakhdar and Gillaizeau recognized the generation of phosphinoyl radicals from the combination of diphenyliodonium salts with triethylamine (Et_3N) in phosphorylations.[9] Despite these elegant advances, the utility of diaryliodonium salts in radical processes still remains largely unexplored.



Scheme 1. Arylations and novel reactivity pattern of *ortho*-functionalized diaryliodonium salts.

On the other hand, biarylamines occupy a vital position in fine chemicals.[10] Transition-metal catalyzed traditional coupling reactions (e.g. Suzuki, Kumada, Negeshi, Stille, Ullman reaction, Buchwald-Hartwig) or dehydrogenative couplings in synthesis of steric hindered biaryls always meet difficulties due to both

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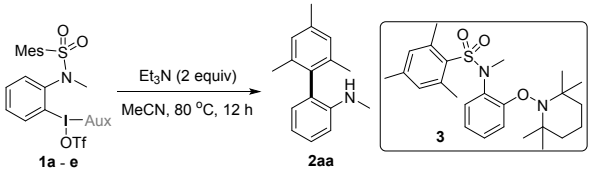
electronic and steric factors (Scheme 1, b).[11] Of note, the intermolecular arylation of aliphatic amines using diaryliodonium salts were reported by Stuart and Olofsson in synthesis of a wide range of arylated amines (Scheme 1, b). However, biarylamines were not described in their reports.[12] In view of the biarylamine synthesis via Ar-Ar bond-forming strategies, the benefit of radical process was generally considered since that steric factors did not affect the reactivity. However, the selectivity was a crucial issue in comparsion with metal-catalyzed coupling reactions.[13] In this regard, diaryliodonium salts allow excellent regioselectivity by adjusting the auxiliary group when aryl radical as a highly reactive intermediate participates in the reactions.[7,12] Recently, our laboratory have uncovered an intramolecular aryl migration of vicinal trifluoromethanesulfonate substituted diaryliodonium salts for the synthesis of steric hindered *ortho*-iodo diaryl ethers (Scheme 1, c).[2d] The novel reactivity pattern of *ortho*-functionalized diaryliodonium salts inspires us to explore the further C-N bond formations. Herein, we present the base-promoted desulfonylation/aryl migration of vicinal aryl sulfonamide substituted diaryliodonium salts via aryl radical induced process (Scheme 1, d). It was worth to mention that biarylamines with steric hindrance are favored by this method.

Table 1. Desulfonylative aryl migration reaction.[a]



Entry	Auxiliary	Scavenger	Yield [%][b]
1	Phenyl (**1a**)	/	86
2	4-Methoxyphenyl (**1b**)	/	64
3	2,4,6-Trimethoxylphenyl (**1c**)	/	53
4	2,4,6-Trimethylphenyl (**1d**)	/	65
5	4-Nitrophenyl (**1e**)	/	20
6[c]	Phenyl (**1a**)	TEMPO	37
7[d]	Phenyl (**1a**)	TEMPO	Trace
8[e]	Phenyl (**1a**)	BHT	Trace

[a] Standard conditions: **1** (0.3 mmol), Et_3N (2 equiv.) in 5 mL MeCN, 80 °C, 12 hours. [b] Isolated yield. [c] TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxyl (2 equiv.). [d] TEMPO (10 equiv.). [e] BHT= Butylated hydroxytoluene (10 equiv.).

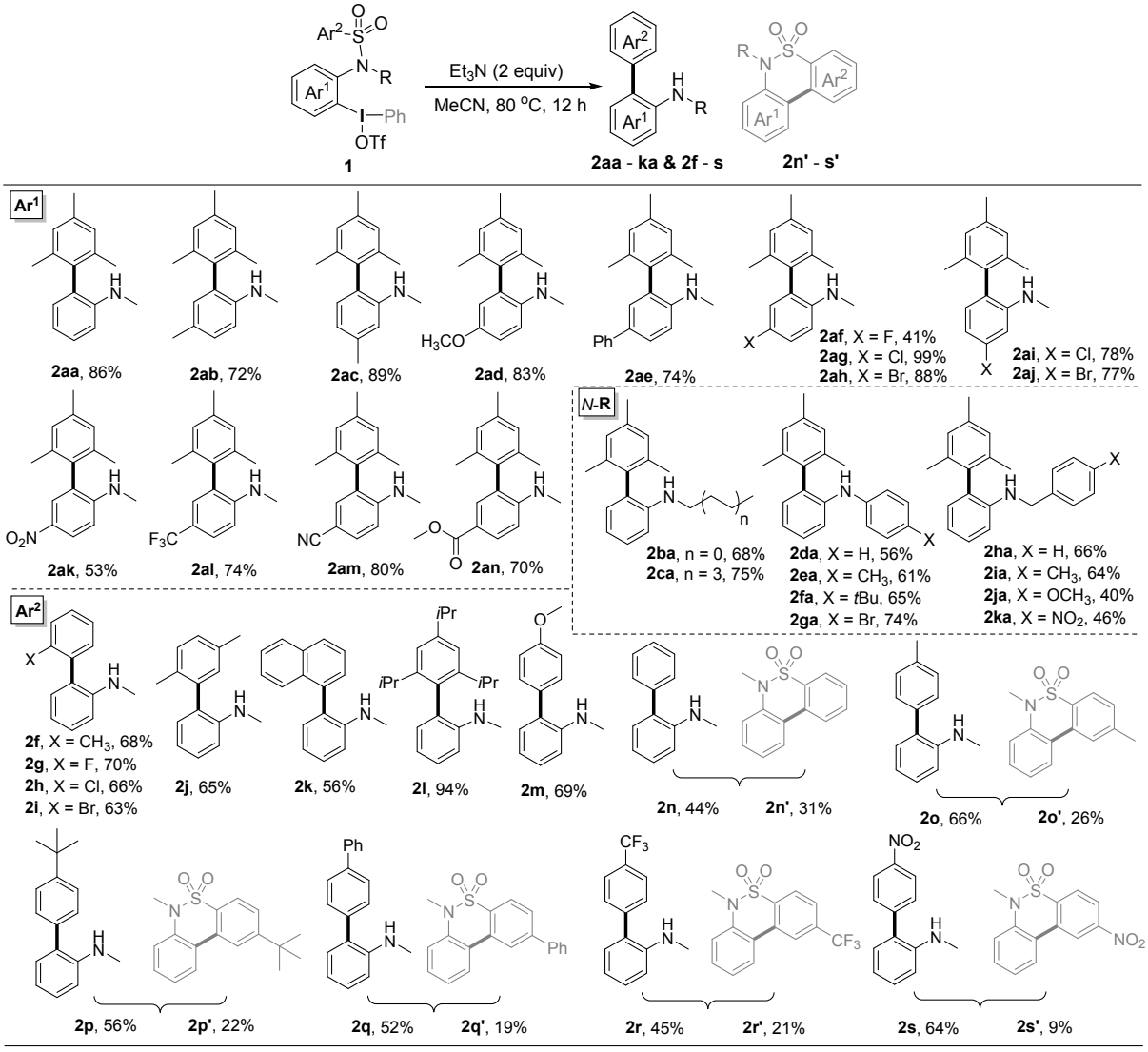
To begin our studies, iodonium triflate (**1a**) was chosen as the model substrate and the desired product **2aa** was isolated in 86% yield when the reaction was performed in the presence of 2.0 equivalent of Et_3N in acetonitrile at 80 °C (Table 1, entry 1).[14] Then several substrates **1b**-**1e** bearing various auxiliary groups were prepared and employed in the reaction. As a result, electron-donating 4-methoxyphenyl and bukyl 2,4,6-trimethylphenyl as auxiliary group gave **2aa** in comparable yields of 64% and 65%, respectively. While 4-nitrophenyl **1e** resulted in a poor yield of 20% (Table 1, entry 5). Specifically, **1c** bearing 2,4,6-trimethoxylphenyl only gave 53% yield of **2aa** (Table 1, entry 3). When the radical scavenger of TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) or BHT (butylated hydroxytoluene) was introduced to the reaction, it was found that the reaction was inhibited by decreasing the yield of **2aa** significantly (Table 1, entries 6-8). Moreover, the radical trapping product **3** in the reaction of **1a** with TEMPO was detected by ESI-MS spectra.[14] To show the effect of reactivity caused by the auxiliary group, EPR spin-trapping experiments were conducted for the reaction of iodonium salts **1a**-**1e** with Et_3N in the presence of *α*-phenyl-*N*-*tert*-butylnitrone (PBN) at room temperature.[14] The EPR spectra revealed the formation of aryl-PBN radical adducts which were characterized by hyperfine coupling constants (a_N = 14.7 G and a_H = 2.6 G).[15] Interestingly, the intensity of **1a** is much larger than the others, which was consistant with the best yield of **2aa**.

We subsequently examined the structural diversity of various *N*-containing iodonium salts by assessing the substitution effects on the aryl motif and *N*-substituents. Firstly, substrates **1** with a broad range of substituents on the benzene ring (Ar^1) were first investigated. As shown in Table 2, electron-neutral, -donating or -withdrawing substituents were generally well-tolerated, affording the desired products **2aa**-**2an** bearing hydrogen (**2aa**), methyl (**2ab** and **2ac**), methoxy (**2ad**), phenyl (**2ae**), halogen (**2af**-**j**), nitro (**2ak**), trifluoromethyl (**2al**), cyano (**2am**) and ester (**2an**) functionalities in good to excellent yields of 41-99%. We next turned our attention to the substituents on the nitrogen of diaryliodonium salts. It was pleased to find that substrates with various R groups also gave the desired biarylamines **2ba**-**2ka** in good yields of 40-75%. Specifically, the reactions went smoothly to afford amines **2ba** and **2ca** bearing alkyl groups in 68% and 75% yields, respectively. Products **2da**-**2ga** with *N*-substituents of aromatic rings were also obtained in 56-74% yields. Moreover, substrates with benzyl or substituted benzyl groups were compatible in this reaction, the amines **2ha**-**2ka** were furnished in 40-66% yields. Then, we sought to examine the scope of diverse aryl sulfonyl groups (Ar^2), the generality of the protocol was also presented in Table 2. Substrates **1** bearing *ortho*-substituted aryls of Ar^2 with steric hindrance were well-tolerated in the reaction and afforded the desired products **2f**-**2k** in the form of single product with yields of 56-70%. Notably, steric demanding iodonium salts facilitate the outcome of the reaction. The case of **2l** bearing 2,4,6-triisopropylphenyl was accomplished in an excellent yield of 94% under the standard conditions. Moreover, iodonium salts **1** with less hindered Ar^2 were also successfully employed in this context. While the sole product of **2m** with electron-donating methoxy group in the *para*-position of Ar^2 was isolated in 69% yield, several pair of products were observed in formation of biarylamines (**2n**-**2s**) along with the cyclic amides (**2n'**-**2s'**), which is consistent with radical chemistry.[16] **2n**-**2s** were isolated in 44-66% yields by *ipso*-substitution together with **2n'**-**2s'** as minor products in 9-31% yields, which can be rationalized in both pathways of *ipso*-substitution and direct radical addition.

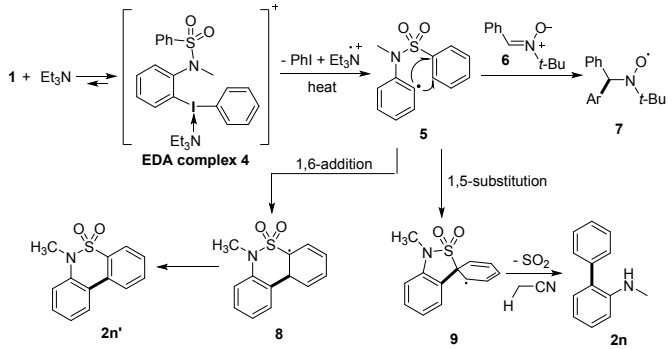
To gain more insights into the plausible radical mechanism, deuteration experiments were carried out in order to determine the source of hydrogen. When the deuterated solvent of MeCN-d_3 was empolyed in the reaction, the signal of *N*-*H* disappeared as shown in ^{1}H-NMR spectra.[14] It implied that the solvent of MeCN served as the hydrogen source. Therefore, a rational reaction pathway is proposed (Scheme 2). Firstly, the association of Et_3N with iodonium salts **1** forms an electron-donor-acceptor (EDA) complex **4**, which was thermally activated

to generate the aryl radical **5** with excellent regioselectivity. EPR spectra confirmed stable radical of **7** which was formed by radical trapping experiment with PBN (**6**). The radical **5** can go through two alternative reaction pathways depending on the substituents of the aryl sulfonyl group.[16] In the formation of cyclic amides, the radical **5** goes [1,6]-addition. The cyclic amide **2n'** was obtained by aromatization from intermediate **8**. Otherwise, a spirocyclic intermediate **9** was generated by [1,5]-substitution, and the desired biarylamine **2n** was formed through desulfonylation and hydrogen abstraction.

Table 2. Scope of diverse *N*-containing diaryliodonium salts.[a]

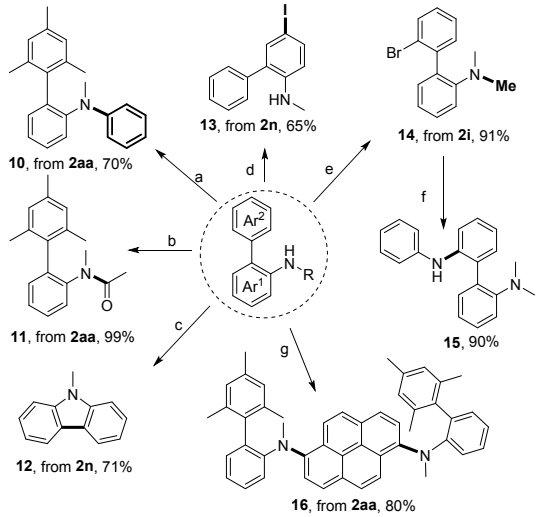


[a] Reaction conditions: diaryliodonium salts **1** (0.3 mmol), Et_3N (0.6 mmol) in 5 mL MeCN, 80 °C, 12 hours; Isolated yield after column chromatography.



Scheme 2. The proposed mechanism.

Next, biarylamines as a family of synthetically versatile synthons were converted into useful aromatic building blocks. As shown in Scheme 3, the N-H group of **2** was easily substituted by phenyl (**10**), acetyl (**11**), and methyl (**14**) groups in excellent yields of 70-99%, in which methyl-substituted biarylamine **14** was further transformed to **15** with aniline in an excellent yield of 90%. Moreover, in the presence of palladium catalysts, the intramolecular coupling reaction furnished **12** in 71% yield. The iodination product **13** was afforded in 65% yield, which could be used as an coupling synthon in further transoformations. To further demonstrate the potential utility of the novel desulfonylation/aryl migration reaction, an attractive molecule **16** was synthesized in 80% yield by double Buchwald-Hartwig coupling reactions with 1,6-dibromopyrene in one pot, which is a potentially useful compound in the field of organic light emitting diodes (OLEDs).[17]



Scheme 3. Derivatization of biarylamines. Reagents and conditions: (a) PhI, $Pd(OAc)_2$/(*t*-Bu)$_3$P, NaO^{t}Bu, toluene, 100 °C; (b) Ac_2O, Et_3N, DMAP, DCM, 25 °C; (c) $Pd(OAc)_2$, $PhI(OAc)_2$, toluene, 25 °C; (d) $Pd(OAc)_2$, $PhI(OAc)_2$, I_2, DCM, 25 °C; (e) HCHO, HCO_2H, 100 °C; (f) $PhNH_2$, $Pd(OAc)_2$/(*t*-Bu)$_3$P, NaO^{t}Bu, toluene, 100 °C; (g) 1,6-dibromopyrene, $Pd(OAc)_2$/(*t*-Bu)$_3$P, NaO^{t}Bu, toluene, 100 °C.

In summary, we have developed a base-promoted desulfonylation/aryl migration cascade of diaryliodonium salts, which provides an efficient route to get access to steric hindered biarylamines. The reaction features wide substrate scope and good functional group tolerance. Further investigation of the detailed reaction mechanism and the application of this transformation are ongoing in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

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