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Letter

Deacetylative Aryl Migration of Diaryliodonium Salts with C(sp^2)–N Bond Formation toward *ortho*-Iodo *N*-Aryl Sulfonamides

Huangguan Chen, Limin Wang, and Jianwei Han*

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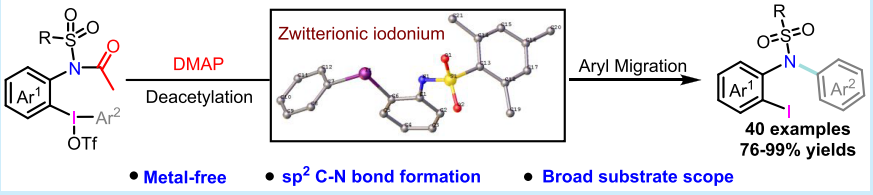
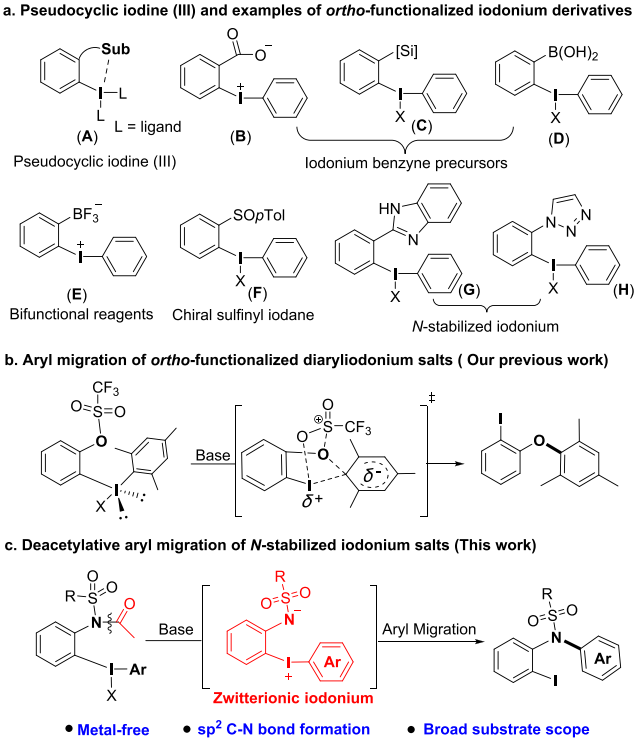


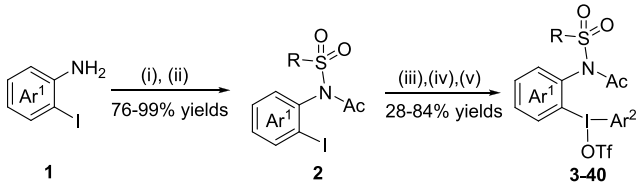
ABSTRACT: An unprecedented approach of metal-free C(sp^2)–N bond formation via deacetylation/intramolecular aryl migration is demonstrated with novel *N*-sulfonamide substituted diaryliodonium salts. The reaction provides a variety of *ortho*-iodo *N*-aryl sulfonamides. The products were employed in several coupling reactions to afford useful diarylamine scaffolds. Furthermore, the key intermediates of zwitterionic iodoniums in the reaction were isolated and verified by the X-ray crystallographic analysis, which showcased unambiguous mechanistic insight into the reactivity of the reaction cascade.

Hypervalent iodine compounds, of which iodine is in high oxidation states (+3 or +5), have aroused widespread

Scheme 1. *ortho*-Functionalized Iodine Reagents and Its Novel Reactivity



Scheme 2. Synthetic Routes to *N*-Substituted Diaryliodonium Salts[a]



[a]Reagents and conditions: (i) RSO_2Cl, pyridine, DCM, 0 to 25 °C; (ii) Ac_2O, DMAP, Et_3N, DCM, 25 °C; (iii) Selectfluor, $CH_3CO_2SiMe_3$, MeCN, 50 °C; (iv) $ArBF_3K$, $CF_3SO_3SiMe_3$ or $CF_3CO_2SiMe_3$, 25 °C; (v) aq. KOTf. DCM = dichloromethane, DMAP = 4-dimethylaminopyridine.

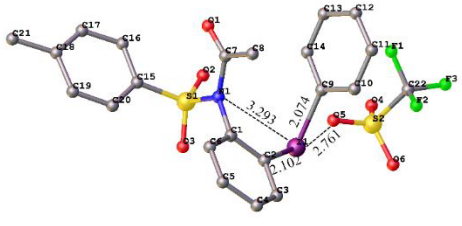


Figure 1. X-ray crystal structural analysis of **30**; protons have been omitted for clarity.

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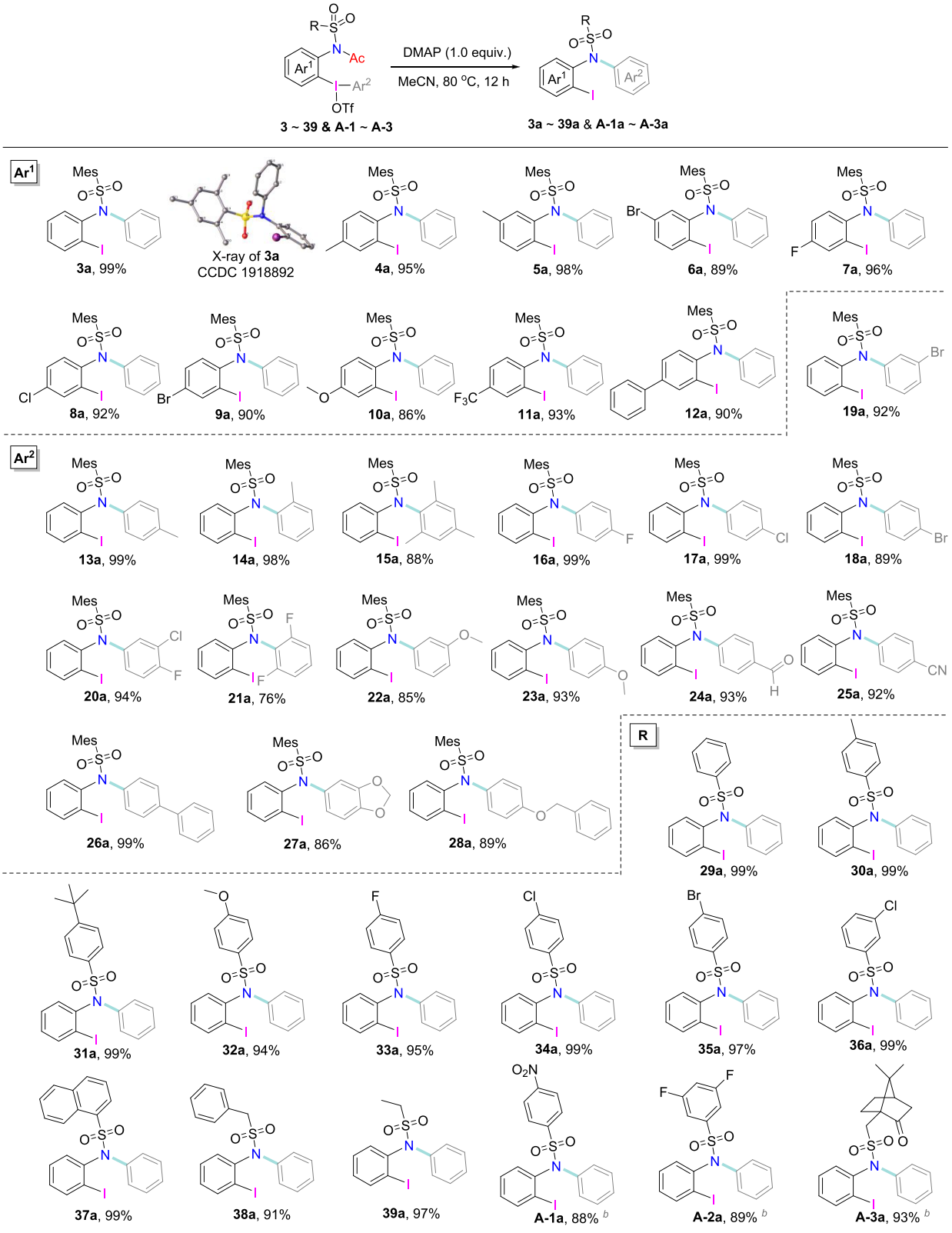
Scheme 3. Scope of Diverse Diaryliodonium Salts for the Synthesis of *ortho*-Iodo *N*-Aryl Sulfonamide[a]



[a]Reaction conditions: diaryliodonium salts (0.3 mmol), DMAP (0.3 mmol) in 5 mL of anhydrous MeCN, 80 °C, 12 h; isolated yield after column chromatography. [b]Zwitterions were employed in the reaction.

interests in the fields of synthetic chemistry and supramolecular studies over the past decades.[1] Structurally, the introduction of a coordinating donor in the *ortho*-position of the phenyliodine-(III) moiety, pioneered by Protasiewicz and co-workers, leads to pseudocyclic iodine(III) compounds with the redirection of secondary bonding at the iodine center (Scheme 1 a, **A**).[2]

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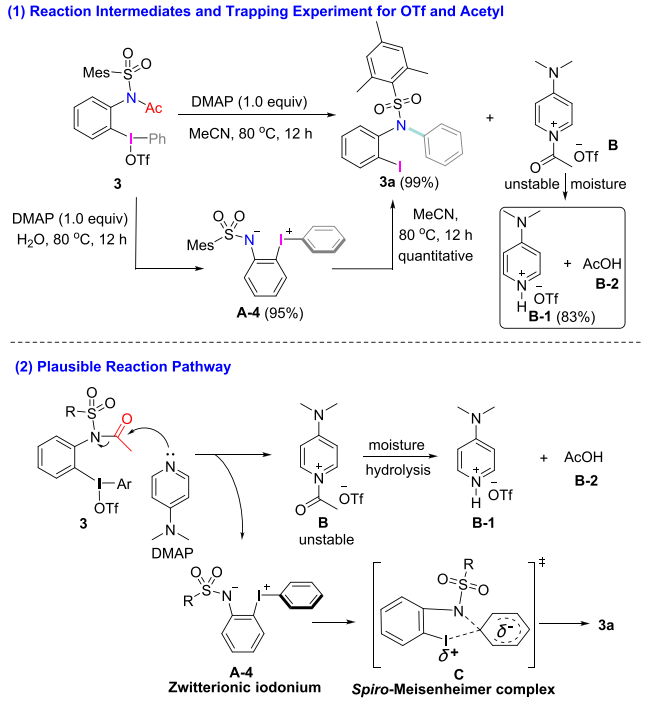
Scheme 4. Mechanistic Investigations



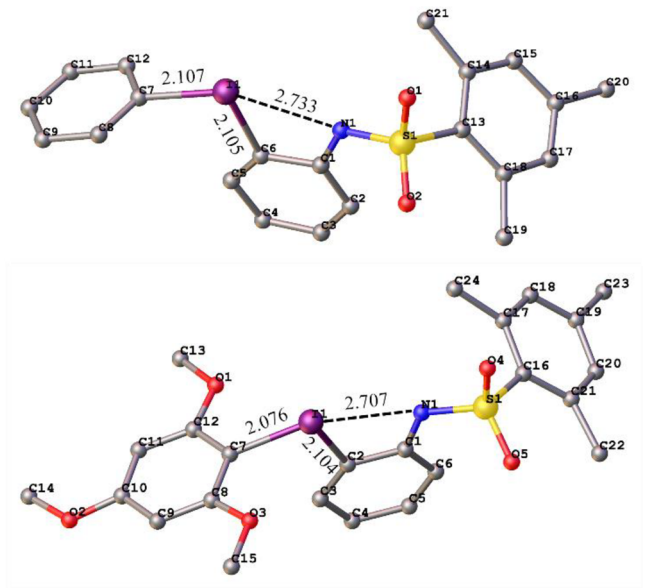
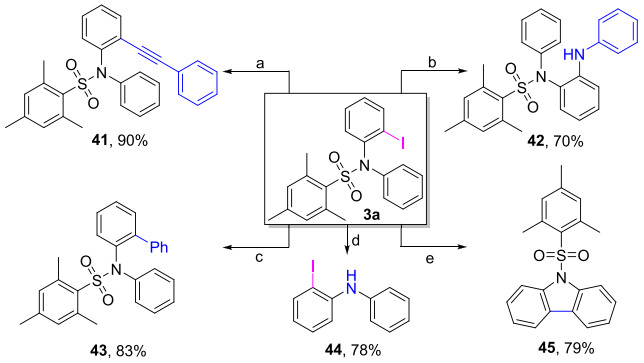


Figure 2. X-ray crystal structures of **A-4** (top) and **A-5** (bottom). Protons have been omitted for clarity.

Pseudocyclic iodine reagents were widely used in synthetic transformations,[3] which also found broad applications in the catalysis and biomimetic reactions.[2b] For example, arylbenziodoxolones, also named diaryliodonium-2-carboxylates, were considered as internal diaryliodonium salts bearing an anionic carboxylate moiety, which emerged as versatile arylating reagents as well as benzyne precursors (Scheme 1 a, **B**).[4] Besides, *ortho*-functionalized diaryliodonium salts such as phenyl[2-(trimethylsilyl)phenyl]iodonium triflate (Kitamura's reagent, Scheme 1a, **C**) and pseudocyclic arylbenziodoxaborole triflates (Scheme 1a, **D**) by Yoshimura and Zhdankin can readily generate benzyne species for the reactions.[5] Notably, Legault reported the new zwitterions of aryliodine(III) bearing a 2-

Scheme 5. Derivatization of *ortho*-Iodo Sulfonamide 3a[a]



[a]Reagents and conditions: (a) Phenylacetylene, $Pd(PPh_3)_4$/CuI, Et_3N, reflux; (b) aniline, $Pd(OAc)_2/(t\text{-}Bu)_3P$, NaO^tBu, toluene, 100 °C; (c) phenylboronic acid, $Pd(PPh_3)_4$, K_2CO_3, DMF, 100 °C; (d) triflic acid, DCE, 0 to 25 °C; (e) $Pd(OAc)_2/PCy_3\text{-}HBF_4$, K_2CO_3, Ag_2CO_3, DMA, 130 °C. DMF = *N*, *N*-dimethylformamide, DCE = 1,2-dichloroethane, DMA = *N*,*N*-dimethylacetamide.

trifluoroborate moiety in the arylation of phenolates (Scheme 1a, **E**).[6] Wencel-Delord and Colobert developed *ortho*-sulfoxide diaryliodonium salts, which enabled C−N coupling reactions with indolines in excellent atropselectivity (Scheme 1a, **F**).[7] It is anticipated that incorporation of the nitrogen atom or *N*-heterocycles as strongly coordinating substituents at the *ortho*-position of the iodonium salts could lead to novel reactivity by easy cleavage of the C−I bond. In sharp contrast, *N*-containing iodonium salts are relatively limited within the family of diaryliodonium salts.[8] Very recently, Zhdankin and Yusubov reported 2-benzimidazolyl substituted diaryliodonum salts, which can further afford five-membered iodine−nitrogen heterocycles with potassium hydroxides (Scheme 1a, **G**).[9a] Simultaneously, Nachtsheim and co-workers independently disclosed 2-triazole stabilized pseudocyclic diaryliodonium salts with aryl-λ^3-iodanes bearing a *N*-heterocycle adjacent to an iodine atom (Scheme 1 a, **H**).[9b]

We hypothesized that the rational design and development of thermally stable *ortho*-functionalized diaryliodonium salts on the basis of structural modifications enable the intramolecular aryl migration. On the basis of this strategy, a family of vicinal trifluoromethanesulfonate substituted iodonium salts were synthesized in our previous work and a series of *ortho*-iodo diaryl ethers were obtained through intramolecular aryl migration (Scheme 1 b).[10] In comparison of C−O bond formation, transition-metal-free C(sp^2)−N coupling is more attractive and challenging.[11] Herein, we describe the strategy of intramolecular deacetylative arylation of *ortho N*-substituted diaryliodonium salts with sp^2 C−N bond formation under metal-free conditions.

First, a family of vicinal *N*-acetyl sulfonamide substituted diaryliodonium salts **3**−**40** were synthesized in two steps from 2-iodoaniline derivatives (**1**) (Scheme 2). The iodonium salts were isolated as thermally stable microcrystalline solids. Their structures were characterized by NMR and mass spectra. Of note, **30** was elucidated with X-ray crystallographic analysis (Figure 1).[12] The distance between the iodine and nitrogen atoms of 3.293 Å was below the sum of their van der Waals radii of 3.53 Å, which indicated a weak secondary bond interaction.[13]

Subsequently, diaryliodonium salts **3** were treated with 4-dimethylaminopyridine (DMAP) in anhydrous acetonitrile at 80 °C for 12 h,[14] and the product **3a** was isolated in 99% yield,

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whose structure was verified by the X-ray crystallographic analysis.[15a] Then the reaction scope was explored (Scheme 3). Iodonium salts **3**−**28** with a variety of substitutions on both Ar^1 and Ar^2 moieties were examined. The reactions proceeded smoothly to afford desired products **3a**−**28a** in excellent yields of 76−99% with tolerance of various functional groups. Next, the sulfonyl moieties were investigated. To our delight, substrates with different sulfonyl groups worked well in this reaction. Benzyl- (**38**) and alkylsulfonyl (**39**) moieties were well tolerated to afford the corresponding products (**38a** and **39a**) in 91% and 97% yields, respectively. Importantly, three stable compounds bearing electron-withdrawing or steric groups, which proved to be zwitterions of **A-1** to **A-3** instead of the iodonium salts, also enable production of the desired products (**A-1a**, **A-2a**, and **A-3a**) in excellent yields of 88−93%.

In order to clarify the reaction mechanism, we carefully examined the formed products in the model reaction. The salt of **B-1** was isolated in 83% yield after column chromatography, and acetic acid **B-2** was detected by the Gas Chromatography−Mass Spectrometry (GC-MS) method. As the reaction was performed under anhydrous conditions, the observation of **B-1** and **B-2** could be derived from the hydrolysis of the extremely unstable *N*-acylpyridinium salt **B**, which was the actual product in the reaction system.[16] More importantly, the zwitterion **A-4** was isolated in 95% yield when **3** was treated with DMAP in water. Further transformation of **A-4** afforded **3a** in quantitative yield (Scheme 4(1)). Undoubtedly, zwitterion **A-4** was considered to be the key intermediate in the reaction. As shown in Figure 2, the structure of **A-4** was fortunately established by the X-ray diffraction,[15b] which provides valuable insights into nitrogen-containing zwitterion or iodonium ylide chemistry.[17] Additionally, a single crystal of zwitterion **A-5** bearing a 2,4,6-trimethoxyphenyl (TMP) group, which was prepared from iodonium salt **40**, was also obtained for crystallographic analysis.[15c] However, zwitterion **A-5** was unable to conduct the aryl immigration under the standard conditions. The I···N length in **A-5** (2.707 Å) is shorter than that of **A-4** (2.733 Å). Notably, the covalent C_7−I bond length of Ar−I in **A-5** (2.076 Å) is significantly shorter than that of **A-4** (2.107 Å) due to the electron-rich aromatic ring of TMP, in which the stable C_7−I bond of **A-5** may account for the inert reactivity of **A-5**.

Based on the above evidence, a plausible reaction pathway was proposed (Scheme 4, 2). Due to the secondary bond interaction of I···N, the amide bond of **3** was fragile enough to cleavage in the presence of DMAP. Thus, the zwitterion **A-4** was formed accompanied by *N*-acylpyridinium salt **B**. **B** was extremely unstable in the presence of moisture and could be hydrolyzed to compound **B-1** and acetic acid **B-2** immediately.[16] The zwitterion **A-4** could undergo aryl migration to afford the desired product **3a** via *spiro*-Meisenheimer complex **C** under thermal conditions.[18] In the case of zwitterion **A-5**, the existence of an ultra-electron-rich moiety of the 2,4,6-trimethoxyphenyl (TMP) group resisted the formation of *spiro*-Meisenheimer complex **C**, which can account for its inert reactivity.

To further demonstrate the potential utilities of the products of *ortho*-iodo *N*-aryl sulfonamides, a series of synthetic manipulations were performed as illustrated in Scheme 5. By utilizing the highly reactive C−I bonds, **3a** was coupled with phenylacetylene (**41**), aniline (**42**), and phenylboronic acid (**43**), and the corresponding new molecules were isolated in good to excellent yields of 70−90%. Besides intermolecular cross-couplings, *ortho*-iodo diarylamine (**44**) and carbazole derivatives (**45**) were furnished in good yields of 78−79% via hydrolysis or intramolecular C−H activation.

In summary, we have disclosed a metal-free sp^2 C−N bond formation strategy via new *N*-substituted diaryliodnium salts to access *ortho*-iodo *N*-aryl sulfonamides. The method features the following: (1) a novel reaction cascade of deacetylation and intramolecular aryl migration; (2) broad functional group tolerance under mild conditions and (3) without wastage of Ar−I residues. More importantly, the zwitterion as an intermediate was definitive evidence to clarify the reaction mechanism. Further investigation of such hypervalent iodine compounds as synthetic reagents are ongoing in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01024.

Experimental procedures, characterization data and spectra of new compounds (PDF)

Accession Codes

CCDC 1918892−1918893, 1918900, and 1918903 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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(14) See the Supporting Information for detailed reaction condition optimization.

(15) (a) CCDC 1918892 contains the supplementary crystallographic data for compound **3a**. (b) CCDC 1918893 is for compound **A-4**. (c) CCDC 1918900 is for compound **A-5**.

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