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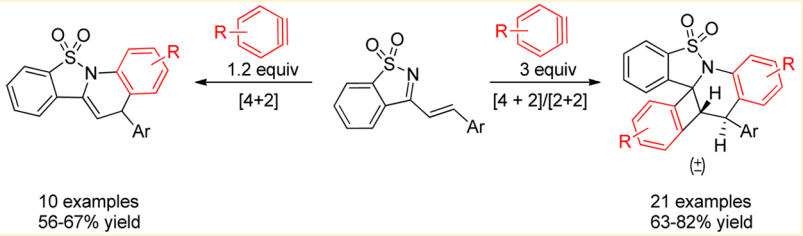
Selective Aza Diels–Alder and Domino [4+2]/[2+2] Cycloaddition Reactions of Arynes with *N*-Sulfonyl Ketimines

I. N. Chaithanya Kiran,[†] R. Santhosh Reddy,[†] Chandraiah Lagishetti, Huacheng Xu, Zhen Wang,* and Yun He*

School of Pharmaceutical Sciences and Innovative Drug Research Centre, Chongqing University, 55 Daxuecheng South Rd., Shapingba, Chongqing 401331, P.R. China

Supporting Information



ABSTRACT: Transition-metal-free inverse electron-demand aza Diels–Alder and domino [4+2]/[2+2] cycloaddition reaction of arynes and *N*-sulfonyl ketimines has been demonstrated. This novel, mild, and efficient protocol allows rapid access to isothiazole dioxide-fused dihydroquinoline or dihydrocyclobutaquinoline derivatives selectively by simply varying the equivalents of aryne precursors. The application of this method has been amply illustrated in the synthesis of 2,4-diarylquinolines.

Cyclic sulfonamides (sultams) are privileged structural motifs, endowed with broad and important biological activities.[1] Among them, benzofused 5-membered sulfonamides have found extensive applications in medicine and received much attention, as they are commonly occurring key structural units of drugs or biologically active compounds, such as HCV (Hepatitis C virus) NS5b inhibitors,[2a] HIV-1 inhibitors,[2b] selective CRTh2 antagonists,[2c] and 5-HT2 receptor antagonists.[2d] Various bioactive sultams are generally constructed from versatile synthetic building block 3-styryl-1,2-benzoisothiazole 1,1-dioxide **1**, which are stable compounds with high electrophilic nature, readily available from saccharins and aldehydes.[3−8] They have been amply utilized for the synthesis of sulfonamide heterocycles via 1,2- and 1,4-additions[4] or [5+3],[5] [4+2],[6] [3+3],[7] [3+2][8] annulations with various reacting partners. In view of its high reactivity and efficiency, further exploration of new reacting partners would be highly desirable for drug discovery research.

The introduction of 2-(trimethylsilyl)aryl triflates (**2**) as mild aryne precursor[9] has witnessed renaissance of interest in aryne chemistry.[10] These highly reactive intermediates have been utilized in Diels–Alder reaction with a wide range of acyclic and cyclic dienes.[11] However, the use of aza dienes for aza Diels–Alder reaction (ADAR) with arynes remained largely unexplored,[12] due to the fact that aryne can react with imines and aza dienes essentially via [2+2] cycloaddition reactions to provide the corresponding benzazetidines.[13] Recently we have reported the synthesis of dihydrophenanthridines using ADAR of ethyl(arylimino)acetate and aryne (Scheme 1, eq 2).[14a] Inspired by literature precedents[12,14a] and in continuation to our efforts on the transition-metal-free synthesis of valuable bioactive scaffolds using arynes[14a−e] through multiple bond-forming transformations[14f−h] (MBFTs), we envisaged that the *N*-sulfonyl ketimines **1** and *in situ* generated aryne could undergo inverse electron-demand (IED) ADAR to afford isothiazole dioxide-fused dihydroquinoline **4** (Scheme 1, eq 3).

During our studies, in addition to the formation of dihydroquinolines **4**, on using excess of arynes the reaction surprisingly underwent an unexpected domino [4+2]/[2+2] process to provide structurally divergent isothiazole dioxide-fused dihydrocyclobutaquinoline **3** as single diastereomer, where the expected dihydroquinoline **4** reacted with excess of aryne via a stereoselective [2+2] cycloaddition. This cascade reaction aroused our curiosity, as domino [4+2]/[2+2] reaction of aryne has received only scant attention and is one of the most powerful methods for preparing structurally divergent polycyclic systems.[15] Indene/benzofuran are known to undergo tandem [4+2]/[2+2] reaction with aryne to provide functionalized dihydrobenzocyclobuta-phenanthrenes (Scheme 1, eq 1).[15a] Herein, we report the transition-metal-free reaction of arynes with 1-sulfonyl-1-azadienes **1** for the synthesis of dihydroquinolines **4** and dihydrocyclobutaquinoline **3** via IED[6a−d,14a,b] ADAR and domino [4+2]/[2+2] reaction respectively, and importantly the product selectivity depends on the equivalents of arynes used.

Our study was initiated by treatment of 1-sulfonyl-1-azadienes **1a** with the aryne generated from the 2-(trimethylsilyl)aryl triflate precursor **2a** (1.2 equiv) using CsF

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Scheme 1. Tandem [4+2]/[2+2] and IED ADAR of Arynes

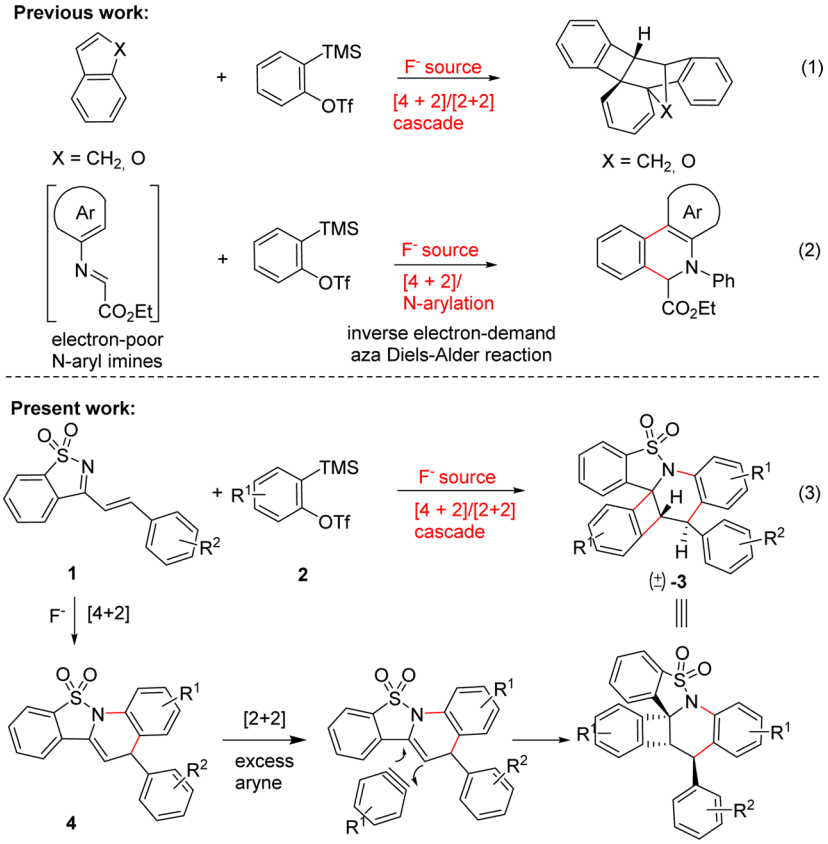
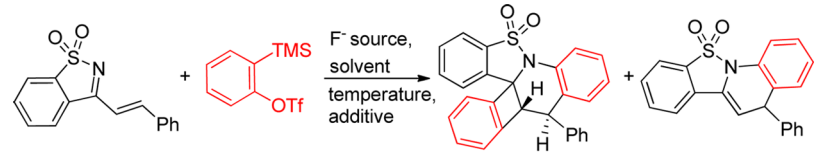


Table 1. Optimization Studies for Reaction of 1-Sulfonyl-1-azadienes with Aryne[a]



entry	2a [equiv]	F⁻ source [equiv]	18-c-6 [equiv]	solvent	time (h)	yield (%)[b] 3a	yield (%)[b] 4a
1	1.25	CsF (2.5)		CH_3CN	12	19	38
2	1.25	KF (2.5)	2.5	CH_3CN	6	8	67
3	1.25	TBAF (2.5)		THF	6	17	31
4	1.25	TBAT (2.5)		THF	6	16	21
5	1.25	CsF (2.5)[c]		CH_3CN	8	13	42
6	1.25	KF (2.5)[c]	2.5	CH_3CN	6	7	58
7	3.00	CsF (5.0)		CH_3CN	16	64	14
8	2.50	KF (5.0)	5.0	CH_3CN	6	74	9
9	3.00	KF (5.0)	5.0	CH_3CN	6	82	6
10	3.50	KF (6.0)	6.0	CH_3CN	6	81	14
11	3.00	TBAF (5.0)		THF	6	45	12
12	3.00	TBAT (5.0)		THF	6	36	18
13	3.00	CsF (5.0)[c]		CH_3CN	12	47	9
14	3.00	KF (5.0)[c]	5.0	CH_3CN	5	68	4

[a]Standard conditions: **1a** (0.20 mmol), **2a**, fluoride source, solvent (3.0 mL). [b]Isolated yields. [c]Reaction temperature 83 °C.

in CH_3CN at room temperature, where the dihydroquinoline **4a** was formed in 38% yield along with 19% of dihydrocyclobutaquinoline **3a** (Table 1, entry 1). Interestingly, when the reaction was performed using KF in the presence of 18-crown-6 as an additive, **4a** was isolated in 67% yield with trace amounts of **3a** (entry 2). The use of other fluoride sources, such as TBAF, did not improve the yield or selectivity (entry 3). When the reaction was carried out using 3 equiv of aryne precursor **2a**, a complete switching in product selectivity from **4a** to **3a** was observed, where **3a** was isolated in 82% yield (entry 9). To

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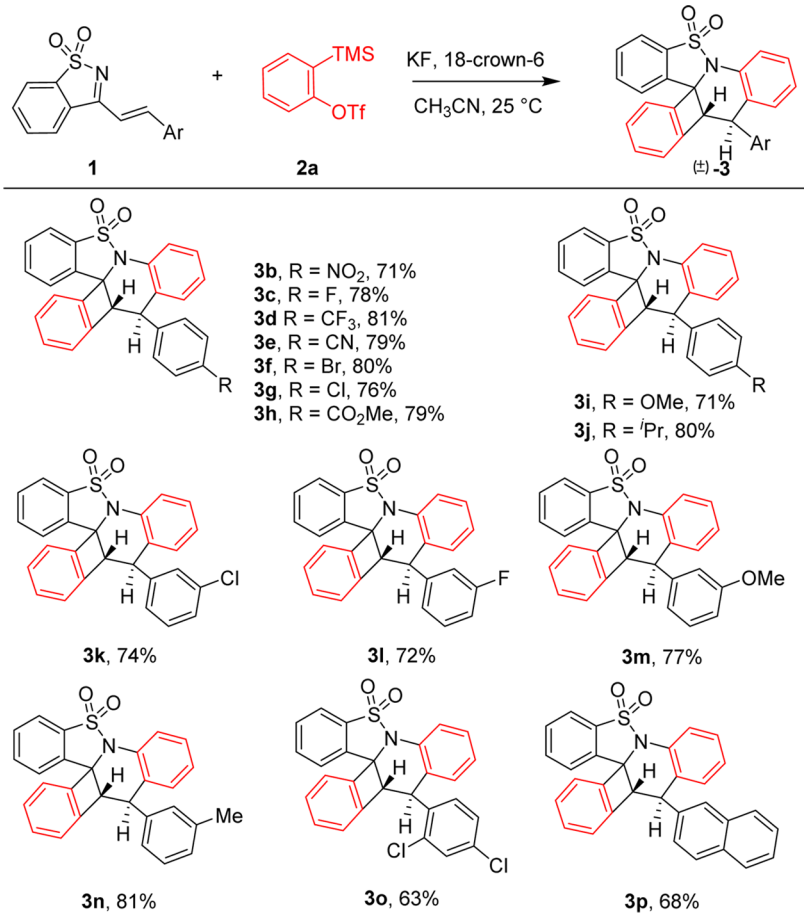
Scheme 2. Substrate Scope of the Domino [4+2]/[2+2] Reaction: Variation of 1-Sulfonyl-1-azadienes[a,b,c]



[a]Reaction conditions: **1** (0.20 mmol), **2a** (0.60 mmol), KF (1.00 mmol), 18-crown-6 (1.00 mmol), CH_3CN (3.0 mL), 25 °C, and 6 h. [b]Yields of the isolated products with respect to **1**. [c]Only negligible amount of [4+2] cycloaddition products observed.

further optimize the yield and selectivity of the products, the effects of fluoride source, temperature, additive, solvent, and stoichiometry were systematically studied (Table 1).

Encouraged by these results, the versatility of domino [4+2]/[2+2] reaction was examined by varying the electronic and steric properties of both 1-sulfonyl-1-azadienes **1** and arynes (Schemes 2 and 3), under the optimized condition (1-azadiene (1.0 equiv), aryne (3.0 equiv), KF (5.0 equiv), 18-crown-6 (5.0 equiv), CH_3CN, 25 °C, 6 h).

As shown in Scheme 2, the domino [4+2]/[2+2] reaction of aryne precursor **2a** with 3-vinyl-1,2-benzoisothiazole 1,1-dioxides (**1**) proceeded effectively to furnish dihydrocyclobutaquinoline derivatives **3** in moderate to excellent yields. The *β*-position of the olefin unit in 1-sulfonyl-1-azadienes **1b−j** bearing both electron-withdrawing (−NO_2, −F, −CF_3, −CN, −Br, −Cl, −CO_2Me) and -donating substituents (−OMe, −^{i}propyl) at *para*-position of phenyl groups were well tolerated, and the corresponding reactions proceeded smoothly to afford the desired dihydroquinolines **3b−j** in 71−81% yields.

Moreover, electron-withdrawing and -donating substituents at the *meta*-position of the aryl ring gave the dihydroquinolines **3k−n** in good yields. Intriguingly, sterically hindered substrates **1o** with 2,4-dichloro-substituted phenyl ring resulted in the desired product **3o** in 63% yield. Further investigation proved that 1-sulfonyl-1-azadiene **1p** with a naphthyl group was also a suitable substrate for this conversion and afforded dihydroquinoline **3p**. It is noteworthy to mention that various halo compounds synthesized could potentially be employed in coupling reactions to afford libraries of dihydrocyclobutaquinolines.

In an attempt to further widen the scope and generality of the domino [4+2]/[2+2] reaction, various substituted 2-(trimethylsilyl)aryl triflates **2** were examined to demonstrate the power of this method to construct molecular diversity and complexity from simple building blocks (Scheme 3).

The parent aryne derived from **2a** reacted with 1-sulfonyl-1-azadienes **1a** to provide quinoline **3a** in 82% yield, the structure and stereochemistry of **3a** was unequivocally confirmed by single-crystal X-ray analysis.[16] 4,5-Disubstituted symmetrical aryne precursors, indane, and dimethyl derivatives reacted smoothly with 1-sulfonyl-1-azadienes to provide the corresponding products (**3q−t**) in good yields. Electronically rich 4,5-benzodioxolebenzyne furnished dihydroquinoline **3u** in 77% yield on reacting with 1-azadiene **1a**. Remarkably, the unsymmetrical 4-methylbenzyne furnished almost equal amounts regioisomeric products (**3v**) in 68% yield. To further investigate the synthetic utility of this reaction, a gram-scale version of the reaction between diene **1a** and aryne **2a** was carried out, and compound **3a** was obtained in 80% yield.

Inspired by the domino [4+2]/[2+2] cycloaddition and its broad substrate scope in the synthesis of polycylic dihydroquinolines **3**, further studies were continued for the selective synthesis of dihydroquinolines **4** via IED ADAR. During optimization studies, it was observed that on using 1.25 equiv

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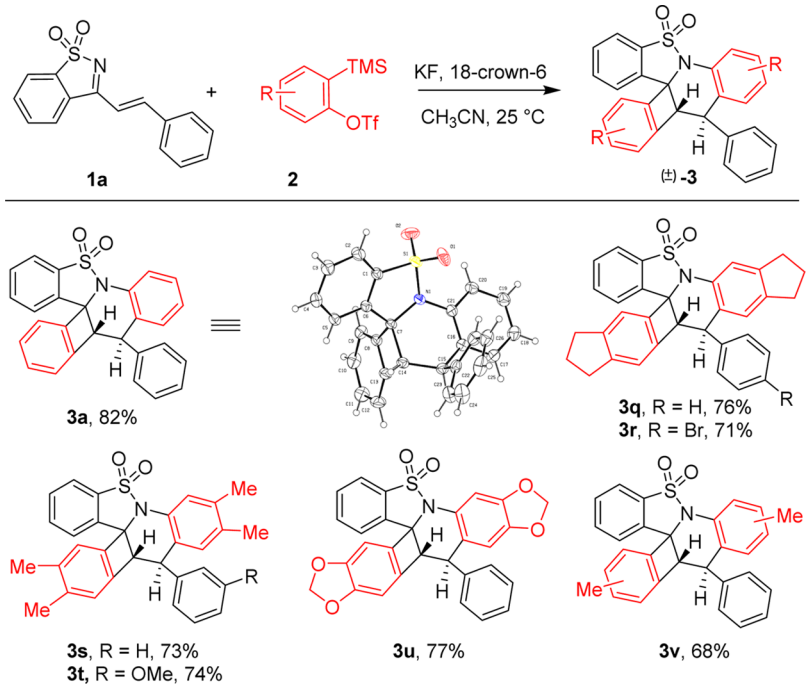
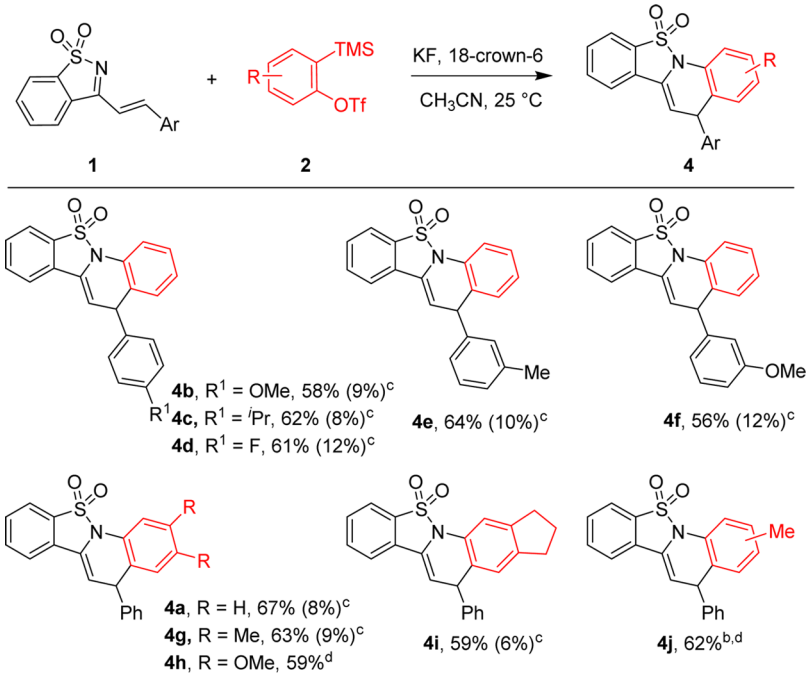
Scheme 3. Substrate Scope of the Domino [4+2]/[2+2] Reaction: Variation of Arynes[a,b,c]



[a]Reaction conditions: **1a** (0.20 mmol), **2** (0.60 mmol), KF (1.00 mmol), 18-crown-6 (1.00 mmol), CH_3CN (3.0 mL), 25 °C, and 6 h. [b]Yields of the isolated products with respect to **1a**. [c]Only negligible amount of [4+2] cycloaddition products observed.

Scheme 4. Substrate Scope of the IED Aza Diels–Alder Reaction: Variation of 1-Sulfonyl-1-azadienes and Arynes[a]



[a]Reaction conditions: **1a** (0.20 mmol), **2** (0.25 mmol), KF (0.50 mmol), 18-crown-6 (0.50 mmol), CH_3CN (3.0 mL), 25 °C, and 6 h. Yields of the isolated products with respect to **1**. [b]Inseparable mixture of regioisomers (2:1) as determined by ^1H NMR. [c]Yield of domino [4+2]/[2+2] product. [d]Only negligible amount of [4+2]/[2+2] product observed.

of aryne **2a** to react with 1-azadiene **1a** (1.0 equiv) in the presence of KF (2.5 equiv) and 18-crown-6 (2.5 equiv) in CH_3CN at 25 °C afforded dihydroquinoline **4a** as the major product.

The scope of this transition-metal-free synthesis of dihydroquinolines **4** was found to be general with various 1-sulfonyl-1-azadienes and differently substituted arynes (Scheme 4). The *β*-position of the olefin unit in cyclic-1-azadienes bearing electron-releasing or -withdrawing substituents at the *para*-position of the aryl ring gave dihydroquinolines **4b–d** in moderate yields. Similarly, electron-donating substituents (−OMe, −Me) at *meta*-position of phenyl groups were also

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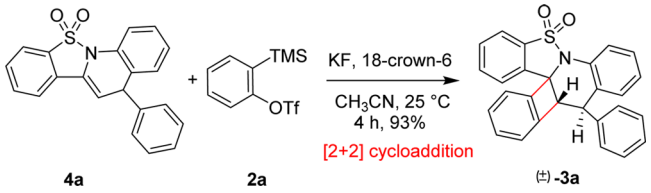
well tolerated, and afforded the desired products **4e−f**. Moreover, parent aryne **2a** and 4,5-disubstituted symmetrical aryne precursors including dimethyl, dimethoxy, and indane derivatives reacted smoothly with 1-sulfonyl-1-azadiene **1a** under optimized reaction condition to provide dihydroquinolines **4a**, **4g−i** in moderate yields. Most notably, unsymmeytical 4-methylbenzyne furnished both the possible regioisomeric products **4j** in 62% yield.

To shed light on the reaction pathway of polycylic dihydroquinolines **3** synthesis and to confirm the mechanism, dihydroquinoline **4a** was reacted with aryne precursor **2a** under similar reaction conditions (Scheme 5). The formation of

Scheme 5. [2+2] Cycloaddition[a]

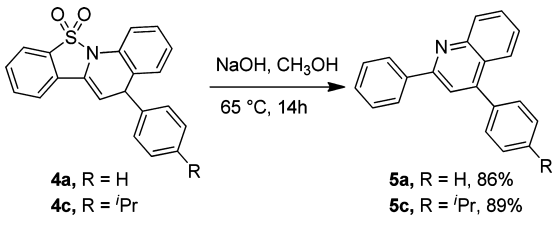


[a]Reaction conditions: **4a** (0.20 mmol), **2a** (0.25 mmol), KF (0.50 mmol), 18-crown-6 (0.50 mmol), CH_3CN (3.0 mL), 25 °C, 4 h.

[2+2] cycloadduct product dihydroquinoline **3a** in 93% yield as single diastereomer confirmed the stepwise ADAR followed by stereoselective [2+2] cycloaddition process.

The synthetic applicability of dihydroquinolines **4** has been demonstrated by the synthesis of 2,4-diarylquinolines. Quinolines are present in the skeleton of a wide number of biologically active compounds that have wide application in the field of medicine and agriculture.[17] Especially, aryl substituted at the 2- or 4-position of quinolines are well-known for their pharmacological properties.[18] Treatment of dihydroquinoline **4a** and **4c** with sodium hydroxide under reflux condition underwent base mediated elimination[19] to provide 2,4-diarylquinoline **5a** and **5c** in 86% and 89% yields respectively (Scheme 6).

Scheme 6. Synthesis of Quinolines[a]



[a]Reaction conditions: **4** (0.10 mmol), NaOH (0.3 mmol), CH_3OH (2.0 mL), 65 °C, and 14 h.

In conclusion, we have developed a mild, general, and efficient inverse electron demand aza Diels−Alder reaction between easily accessible 1-aza-dienes and arynes for the synthesis of isothiazole dioxide-fused dihydroquinolines. In addition, with excess of arynes, the reaction underwent a domino [4+2]/[2+2] cycloaddition to provide dihydrocyclobutaquinolines in a single step with one C−N and three C−C bond formations, demonstrating potential flexibility of the method in formation of molecular diversity. The application of this method has been amply demonstrated in the synthesis of 2,4-diarylquinolines.

EXPERIMENTAL SECTION

General Methods. For product purification by column chromatography, silica gel (200−300 mesh) and hexanes (bp. 60−90 °C) were used unless otherwise indicated. All solvents were dried by standard techniques and distilled prior to use. ^1H NMR and ^{13}C NMR (400, 600 and 101, 151 MHz, respectively) spectra were recorded in $CDCl_3$. ^1H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet and m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.00 ppm). IR spectra reported in terms of frequency of absorption (cm^{-1}). The cyclic 1-azadienes **1**[20] and aryne precursors **2**[21] were prepared according to the literature procedures.

General Procedure for the Domino [4+2]/[2+2] Reaction Involving N-Sulfonyl Ketimines and Arynes. To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the 18-crown-6 (263 mg, 1.00 mmol, 5.0 equiv) and KF (59 mg, 1.00 mmol, 5.0 equiv) under argon atmosphere, then *N*-sulfonyl ketimine **1** (0.20 mmol, 1.0 equiv) was added and the screw-capped tube was evacuated and backfilled with argon. The mixture was dissolved in CH_3CN (3.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at room temperature for 5 min. To the stirring solution was added *β*-trimethylsilyltriflate **1** (0.6 mmol, 3.0 equiv) dropwise, further allowed to stir for 6 h. Then mixture was diluted with CH_2Cl_2 (5.0 mL) and the solvent was evaporated. Subsequently, the crude residue was purified by flash column chromatography on silica gel to afford the corresponding isothiazole dioxide fused dihydrocyclobutaquinoline derivatives **3a−3u** in good yields.

*9-Phenyl-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]-isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3a**).* White solid (0.070 g, 82% yield, mp 170.6−172.4 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3477, 3416, 1639, 1619, 1370, 1271, 699 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 5.4, 3.4 Hz, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.52 (dd, J = 5.7, 3.1 Hz, 2H), 7.36 (q, J = 7.7 Hz, 2H), 7.26−7.19 (m, 4H), 7.16 (d, J = 4.3 Hz, 4H), 7.09−7.00 (m, 3H), 4.81 (s, 1H), 4.62 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.7, 144.5, 142.9, 137.6, 134.7, 133.3, 132.4, 130.8, 130.7, 129.7, 128.6, 128.3, 127.4, 126.5, 125.5, 123.4, 122.1, 121.9, 121.2, 120.9, 69.8, 62.9, 49.3; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{19}NO_2SNa^+$ 444.1028, Found 444.1026.

*9-(4-Nitrophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo-[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3b**).* Yellow solid (0.066 g, 71% yield, mp 205.4−207.2 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 3:2); IR (film) ν_{max} 3488, 1633, 1518, 1348, 1176, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.00 (d, J = 8.5 Hz, 2H), 7.91−7.81 (m, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.59 (dd, J = 5.0, 3.3 Hz, 2H), 7.36 (s, 2H), 7.30−7.26 (m, 5H), 7.18 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.3 Hz, 1H), 7.01 (d, J = 7.4 Hz, 1H), 4.77 (s, 1H), 4.69 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 149.9, 144.3, 143.9, 137.1, 134.7, 133.6, 132.7, 130.9, 130.8, 130.1, 129.3, 129.2, 128.6, 126.1, 123.9, 123.4, 122.3, 122.1, 121.7, 121.5, 69.8, 62.9, 49.1 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}N_2O_4SNa^+$ 489.0879, Found 489.0875.

*9-(4-Fluorophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3c**).* Yellow solid (0.069 g, 78% yield, mp 171.1−173.2 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3474, 3422, 1636, 1508, 1305, 1176, 792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.87−7.85 (m, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.52 (dd, J = 5.4, 3.1 Hz, 2H), 7.34−7.30 (m, 2H), 7.24−7.15 (m, 4H), 7.08 (dd, J = 7.6, 5.8 Hz, 2H), 7.04−6.96 (m, 2H), 6.80 (t, J = 8.6 Hz, 2H), 4.74 (s, 1H), 4.58 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.3 (d, $^1J_{C-F}$ = 245.1 Hz), 144.5, 144.3, 138.5, 137.4, 134.6, 133.3, 132.4, 130.7, 130.6, 129.7 (d, $^3J_{C-F}$ = 10.6 Hz), 129.1, 128.9, 128.4, 125.7, 123.4, 122.0, 121.1, 115.3 (d, $^2J_{C-F}$ = 21.3 Hz), 69.8, 63.1, 48.4 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}FNO_2SNa^+$ 462.0934, Found 462.0937.

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*9-(4-(Trifluoromethyl)phenyl)-8b,9-dihydrobenzo[3,4]cyclobuta-[1,2b]benzo[4,5]isothiazolo [2,3-a]quinoline 15,15-Dioxide (**3d**).* Yellow solid (0.079 g, 81% yield, mp 97.7−100.8 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3417, 1619, 1326, 1273, 1161, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90−7.88 (m, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.58−7.54 (m, 2H), 7.37 (dd, J = 16.1, 7.1 Hz, 4H), 7.26−7.24 (m, 5H), 7.17 (d, J = 7.5 Hz, 1H), 7.04−6.98 (m, 2H), 4.76 (s, 1H), 4.65 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.8, 144.4, 144.2, 137.3, 134.7, 133.5, 132.5, 130.9, 130.8, 129.9, 129.8, 128.8, 127.9, 125.8, 125.7 (q, $^3J_{C-F}$ = 3.4 Hz), 123.9 (q, $^1J_{C-F}$ = 272.2 Hz), 123.4, 122.2, 122.0, 121.4, 121.3, 69.8, 62.8, 49.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{28}H_{18}F_3NO_2SNa^+$ 512.0902, Found 512.0899.

*4-(15,15-Dioxido-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo-[4,5]isothiazolo[2,3-a]quinolin-9-yl)benzonitrile (**3e**).* White solid (0.070 g, 79% yield, mp 149.2−151.8 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3474, 3419, 2228, 1637, 1305, 1176 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 5.7, 3.1 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.59−7.55 (m, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 4.3 Hz, 2H), 7.28−7.22 (m, 5H), 7.16 (d, J = 7.0 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 6.99 (d, J = 7.5 Hz, 1H), 4.75 (s, 1H), 4.65 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 147.9, 144.2, 143.9, 137.1, 134.6, 133.5, 132.6, 132.4, 130.9, 130.8, 130.1, 130.0, 129.4, 129.0, 128.4, 125.9, 123.4, 122.2, 122.1, 121.5, 121.4, 118.6, 110.5, 69.8, 62.8, 49.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{28}H_{18}N_2O_2SNa^+$ 469.0981, Found 469.0977.

*9-(4-Bromophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3f**).* Yellow solid (0.080 g, 80% yield, mp 147.2−149.5 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3452, 1633, 1454, 1304, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86 (dd, J = 5.4, 3.1 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.53 (dd, J = 5.6, 3.0 Hz, 2H), 7.34−7.30 (m, 2H), 7.23 (d, J = 6.3 Hz, 5H), 7.13 (t, J = 7.8 Hz, 1H), 7.04−6.96 (m, 4H), 4.72 (s, 1H), 4.55 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.3, 141.8, 137.4, 134.7, 133.4, 132.5, 131.7, 130.8, 130.7, 130.1, 129.9, 129.8, 129.3, 128.6, 125.7, 123.4, 122.2, 122.0, 121.3, 121.2, 120.5, 69.8, 62.9, 48.7 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}BrNO_2SNa^+$ 522.0133, Found 522.0129.

*9-(4-Chlorophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3g**).* Colorless solid (0.069 g, 76% yield, mp 149.2−151.8 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3471, 3422, 1636, 1490, 1306, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 5.6, 3.2 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.55 (dd, J = 5.7, 3.1 Hz, 2H), 7.34 (d, J = 4.2 Hz, 2H), 7.25−7.20 (m, 3H), 7.16−7.14 (m, 1H), 7.12−7.09 (m, 2H), 7.06−7.01 (m, 3H), 6.99 (d, J = 7.5 Hz, 1H), 4.73 (s, 1H), 4.56 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.4, 141.2, 137.4, 134.7, 133.4, 132.5, 132.3, 130.8, 130.2, 129.9, 129.8, 128.9, 128.7, 128.6, 125.7, 123.4, 122.2, 122.0, 121.3, 121.2, 69.8, 63.0, 48.7 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}ClNO_2SNa^+$ 478.0639, Found 478.0635.

*Methyl 4-(15,15-dioxido-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]isothiazolo[2,3-a]quinolin-9-yl)benzoate (**3h**).* Colorless solid (0.076 g, 79% yield, mp 217.8−219.1 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3457, 1718, 1636, 1282, 1177, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89−7.87 (m, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 7.9 Hz, 1H), 7.55 (dd, J = 5.8, 3.1 Hz, 2H), 7.35 (d, J = 4.5 Hz, 2H), 7.26−7.23 (m, 3H), 7.20−7.17 (m, 3H), 7.06−6.99 (m, 2H), 4.78 (s, 1H), 4.64 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.7, 147.8, 144.4, 144.3, 137.3, 134.8, 133.4, 132.6, 130.8, 130.0, 129.9, 129.8, 128.7, 128.4, 127.6, 125.8, 123.4, 122.2, 122.0, 121.3, 121.2, 69.8, 62.9, 51.9, 49.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{29}H_{21}NO_4SNa^+$ 502.1083, Found 502.1079.

*9-(4-Methoxyphenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3i**).* Colorless solid (0.064 g, 71% yield, mp 111.2−113.3 °C); R_f = 0.3 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3457, 3416, 1638, 1304, 1160, 610 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86 (dd, J = 5.8, 2.9 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.51 (dd, J = 5.8, 3.1 Hz, 2H), 7.35−7.29 (m, 2H), 7.24−7.14 (m, 4H), 7.05−6.96 (m, 4H), 6.66 (d, J = 8.7 Hz, 2H), 4.74 (s, 1H), 4.54 (s, 1H), 3.61 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.0, 144.7, 144.5, 137.6, 135.1, 134.7, 133.3, 132.3, 131.0, 130.7, 130.6, 129.7, 129.6, 128.5, 128.2, 125.6, 123.4, 122.1, 121.9, 121.2, 120.9, 113.9, 69.8, 63.1, 55.0, 48.5 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{28}H_{21}NO_3SNa^+$ 474.1134, Found 474.1131.

*9-(4-Isopropylphenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3j**).* White solid (0.074 g, 80% yield, mp 110.7−112.4 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3475, 3418, 1636, 1621, 1176, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.94−7.92 (m, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.59−7.57 (m, 2H), 7.34 (brs, 2H), 7.23−7.17 (m, 4H), 7.05−6.98 (m, 6H), 4.77 (s, 1H), 4.53 (s, 1H), 2.75 (dt, J = 13.8, 6.8 Hz, 1H), 1.12 (d, J = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 147.0, 144.8, 144.7, 140.5, 137.8, 134.9, 133.3, 132.3, 131.0, 130.8, 130.7, 129.8, 129.7, 128.3, 127.3, 126.8, 125.5, 123.5, 122.2, 121.9, 121.3, 120.9, 69.8, 62.8, 49.3, 33.5, 23.8 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{30}H_{26}NO_2S^+$ 464.1679, Found 464.1673.

*9-(3-Chlorophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3k**).* White solid (0.067 g, 74% yield, mp 183.6−185.7 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3454, 1633, 1303, 1159, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.91−7.89 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.59−7.54 (m, 2H), 7.35−7.34 (m, 2H), 7.28−7.20 (m, 3H), 7.16 (d, J = 2.4 Hz, 2H), 7.07−6.99 (m, 4H), 6.96−6.94 (m, 1H), 4.75 (s, 1H), 4.56 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.7, 144.4, 144.3, 137.4, 134.8, 134.2, 133.4, 132.5, 130.8, 130.0, 129.9, 129.8, 128.7, 127.9, 126.8, 125.8, 125.6, 123.4, 122.2, 122.0, 121.4, 69.8, 62.9, 48.9 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}ClNO_2SNa^+$ 478.0639, Found 478.0635.

*9-(3-Fluorophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3l**).* Colorless solid (0.063 g, 72% yield, mp 237.6−239.8 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3475, 3417, 1637, 1489, 1304, 789 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89−7.87 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.56−7.54 (m, 2H), 7.34 (d, J = 4.1 Hz, 2H), 7.25−7.22 (m, 3H), 7.17 (d, J = 7.5 Hz, 1H), 7.11−6.98 (m, 3H), 6.86 (t, J = 8.0 Hz, 2H), 6.75 (t, J = 8.3 Hz, 1H), 4.77 (s, 1H), 4.58 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.7 (d, $^1J_{C-F}$ = 246.2 Hz), 145.2, 144.4, 137.4, 134.8, 133.4, 132.5, 130.8, 130.1, 129.8 (d, $^3J_{C-F}$ = 7.6 Hz), 128.7, 125.7, 123.4, 123.0, 122.2, 122.0, 121.3, 121.3, 114.6 (d, $^2J_{C-F}$ = 22.0 Hz), 113.5 (d, $^2J_{C-F}$ = 21.0 Hz), 69.8, 62.8, 48.9 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{18}FNO_2SNa^+$ 462.0934, Found 462.0931.

*9-(3-Methoxyphenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3m**).* Colorless solid (0.070 g, 77% yield, mp 176.8−179.7 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 3:2); IR (film) ν_{max} 3444, 1631, 1305, 1177, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.84 (dd, J = 5.8, 2.8 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.49−7.47 (m, 2H), 7.36−7.28 (m, 2H), 7.24 (d, J = 3.3 Hz, 1H), 7.20−7.13 (m, 3H), 7.04 (t, J = 8.2 Hz, 1H), 6.96 (t, J = 7.6 Hz, 2H), 6.79 (d, J = 7.6 Hz, 1H), 6.59 (d, J = 5.8 Hz, 2H), 4.78 (s, 1H), 4.55 (s, 1H), 3.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.7, 144.8, 144.5, 144.4, 137.6, 134.8, 133.3, 132.1, 130.8, 130.7, 130.5, 129.7, 129.6, 129.5, 128.3, 125.4, 123.5, 122.1, 121.9, 121.0, 120.7, 119.7, 113.2, 111.7, 69.7, 62.6, 54.8, 49.4 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{28}H_{21}NO_3SNa^+$ 474.1134, Found 474.1130.

*9-(m-Tolyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]benzo[4,5]-isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3n**).* Colorless solid (0.071 g, 81% yield, mp 181.2−183.7 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3475, 3416, 1618, 1491, 1305, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86−7.83 (m, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.48−7.46 (m, 2H), 7.35−7.29 (m, 2H), 7.22−7.14 (m, 4H), 7.02−6.93 (m, 5H), 6.85 (d, J = 7.3 Hz, 1H), 4.75 (s, 1H), 4.54 (s, 1H), 2.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.7, 144.5, 142.9, 138.2, 137.6, 134.8, 133.2, 132.3, 130.9, 130.7, 130.6, 129.7, 129.6, 128.5, 128.2, 127.2, 125.5, 124.4, 123.4, 122.1, 121.9, 121.1, 120.9, 69.8, 63.1, 49.3, 21.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{28}H_{21}NO_2SNa^+$ 458.1185, Found 458.1182.

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*9-(2,4-Dichlorophenyl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3o**).* Yellow solid (0.062 g, 63% yield, mp 237.1−239.3 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3444, 2350, 1632, 1310, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86 (dd, J = 5.4, 3.2 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.53 (dd, J = 5.6, 3.0 Hz, 2H), 7.42−7.23 (m, 4H), 7.25 (t, J = 7.4 Hz, 1H), 7.17 (dd, J = 5.5, 3.0 Hz, 1H), 7.13 (d, J = 6.9 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.98 (dd, J = 10.6, 4.3 Hz, 2H), 6.89 (d, J = 8.5 Hz, 1H), 5.01 (s, 1H), 4.57 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.5, 138.5, 137.5, 134.3, 133.6, 133.5, 133.3, 133.1, 131.3, 130.9, 130.8, 129.9, 129.2, 129.1, 127.7, 126.1, 123.5, 122.1, 121.6, 121.3, 69.6, 61.5, 45.4 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{27}H_{17}Cl_2NO_2SNa^+$ 512.0249, Found 512.0246.

*9-(Naphthalen-2-yl)-8b,9-dihydrobenzo[3,4]cyclobuta[1,2-b]-benzo[4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3p**).* Colorless solid (0.064 g, 68% yield, mp 205.8−207.6 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3445, 1635, 1490, 1305, 1159, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89−7.85 (m, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.58−7.56 (m, 1H), 7.51 (t, J = 4.3 Hz, 3H), 7.40−7.32 (m, 5H), 7.26−7.21 (m, 4H), 7.04 (t, J = 8.0 Hz, 2H), 4.84 (s, 1H), 4.74 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.7, 144.6, 140.2, 137.6, 134.8, 133.4, 133.3, 132.6, 132.0, 130.9, 130.7, 130.6, 129.8, 129.7, 128.5, 128.4, 127.9, 127.2, 126.2, 126.0, 125.9, 125.7, 125.6, 123.4, 122.2, 122.0, 121.3, 121.2, 69.9, 63.2, 49.5 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{31}H_{21}NO_2SNa^+$ 494.1185, Found 494.1181.

*10-Phenyl-6,7,8,9b,10,12,13,14-octahydrobenzo[4,5]isothiazolo-[2,3-a]cyclopenta [g]indeno [5′,6′:3,4]cyclobuta[1,2-b]quinoline 17,17-Dioxide (**3q**).* White solid (0.076 g, 76% yield, mp 236.5−238.3 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3474, 3416, 1639, 1308, 1180, 620 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86 (dd, J = 5.9, 2.6 Hz, 1H), 7.54 (s, 1H), 7.49−7.46 (m, 2H), 7.24−7.19 (m, 2H), 7.13−7.09 (m, 4H), 7.05−7.01 (m, 2H), 6.83 (s, 1H), 4.61 (s, 1H), 4.52 (s, 1H), 2.91−2.71 (m, 8H), 1.97−1.94 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.8, 145.5, 144.5, 143.9, 142.4, 142.1, 141.5, 138.4, 134.8, 133.1, 130.3, 129.5, 128.6, 128.4, 127.5, 126.5, 126.3, 123.4, 121.2, 118.1, 118.0, 117.0, 69.0, 61.7, 49.7, 33.2, 32.9, 32.7, 32.3, 25.3, 25.0 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{33}H_{27}NO_2SNa^+$ 524.1654, Found 524.1651.

*10-(4-Bromophenyl)-6,7,8,9b,10,12,13,14-octahydrobenzo[4,5]-isothiazolo[2,3-a]cyclopenta [g]indeno[5′,6′:3,4]cyclobuta[1,2-b]-quinoline 17,17-Dioxide (**3r**).* Pale yellow solid (0.082 g, 71% yield, mp 167.5−169.7 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3475, 3415, 1638, 1619, 1487, 1307, 1212, 952 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.88−7.85 (m, 1H), 7.54−7.51 (m, 3H), 7.25−7.17 (m, 4H), 7.03−6.97 (m, 3H), 6.82 (s, 1H), 4.54 (s, 1H), 4.47 (s, 1H), 2.88−2.71 (m, 8H), 2.03−1.98 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.9, 145.7, 144.8, 142.7, 142.0, 141.9, 141.7, 138.2, 134.7, 133.2, 131.6, 130.3, 129.6, 129.4, 127.9, 126.5, 123.4, 121.2, 120.2, 118.1, 118.0, 117.2, 69.0, 61.8, 49.1, 33.3, 32.9, 32.7, 32.4, 32.3, 25.3, 25.0 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{33}H_{26}BrNO_2SNa^+$ 602.0760, Found 602.0756.

*6,7,11,12-Tetramethyl-9-phenyl-8b,9-dihydrobenzo[3,4]-cyclobuta[1,2-b]benzo[4,5] isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3s**).* White solid (0.070 g, 73% yield, mp 234.4−237.6 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3476, 3416, 1619, 1489, 1170, 618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.85 (dd, J = 6.1, 2.7 Hz, 1H), 7.48 (dd, J = 6.0, 2.8 Hz, 2H), 7.43 (s, 1H), 7.19 (dd, J = 6.0, 2.7 Hz, 1H), 7.12 (d, J = 4.5 Hz, 5H), 7.05−7.01 (m, 1H), 6.91 (s, 1H), 6.75 (s, 1H), 4.64 (s, 1H), 4.48 (s, 1H), 2.21 (s, 3H), 2.16 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.8, 142.3, 142.1, 139.6, 138.4, 138.2, 136.7, 134.8, 133.9, 133.1, 131.9, 129.8, 129.5, 128.6, 127.8, 127.5, 126.3, 123.4, 122.7, 122.0, 121.8, 69.6, 62.8, 49.1, 20.6, 20.4, 19.5, 19.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{31}H_{27}NO_2SNa^+$ 500.1654, Found 500.1651.

*9-(3-Methoxyphenyl)-6,7,11,12-tetramethyl-8b,9-dihydrobenzo-[3,4]cyclobuta[1,2-b]benzo [4,5]isothiazolo[2,3-a]quinoline 15,15-Dioxide (**3t**).* White solid (0.075 g, 74% yield, mp 124.6−126.8 °C); R_f = 0.3 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3473, 3416, 1639, 1620, 1306, 1160, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89 (dd, J = 5.5, 3.1 Hz, 1H), 7.54 (dd, J = 5.6, 3.0 Hz, 2H), 7.42 (s, 1H), 7.25−7.22 (m, 1H), 7.14−7.10 (m, 2H), 6.93 (s, 1H), 6.78 (d, J = 4.9 Hz, 2H), 6.60 (d, J = 8.1 Hz, 2H), 4.64 (s, 1H), 4.44 (s, 1H), 3.48 (s, 3H), 2.23 (s, 3H), 2.18 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 159.8, 145.8, 142.2, 142.1, 139.7, 138.5, 138.4, 136.7, 134.9, 133.8, 133.2, 131.9, 129.6, 129.5, 127.7, 123.6, 122.7, 121.9, 121.1, 119.8, 113.1, 111.8, 69.5, 62.5, 54.9, 49.3, 20.7, 20.4, 19.6, 19.3 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{32}H_{29}NO_3SNa^+$ 530.1760, Found 530.1755.

*10-Phenyl-9b,10-dihydro-[1,3]dioxolo[4″,5″:4′,5′]benzo-[1′,2′:3,4]cyclobuta[1,2-b]benzo [4,5]isothiazolo[2,3-a][1,3]dioxolo-[4,5-g]quinoline 17,17-Dioxide (**3u**).* Colorless solid (0.078 g, 77% yield, mp 178.6−180.9 °C); R_f = 0.3 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3445, 1632, 1458, 1305, 1213, 1037 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.86−7.84 (m, 1H), 7.53−7.52 (m, 2H), 7.24−7.22 (m, 2H), 7.16−7.05 (m, 5H), 6.81 (s, 1H), 6.64 (s, 1H), 6.47 (s, 1H), 5.88 (s, 2H), 5.86 (s, 2H), 4.51 (s, 1H), 4.38 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 149.9, 148.9, 147.4, 145.5, 142.6, 137.6, 137.5, 136.0, 134.7, 133.3, 129.8, 128.5, 127.5, 126.5, 125.7, 124.0, 123.4, 121.3, 110.3, 103.3, 103.3, 101.4, 100.7, 68.7, 61.4, 49.5 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{29}H_{19}NO_6SNa^+$ 532.0825, Found 532.0822.

*9,13-Dimethyl-11-phenyl-11,11a-dihydrobenzo[3,4]cyclobuta-[1,2-b]benzo[4,5]isothiazolo[2,3-a]quinoline 5,5-Dioxide and Isomers (**3v**).* White solid (0.061 g, 68% yield, mp 113.7- 115.1 °C (inseparable mixture of isomers)); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3058, 3026, 2995, 2992, 1614, 1494, 1453, 1306, 1176, 816, 757, 736, 700, 565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.94−7.86 (m, 3H), 7.65−7.46 (m, 8H), 7.25−7.19 (m, 2H), 7.18−7.10 (m, 8H), 7.10−6.97 (m, 6H), 6.91−6.80 (m, 3H), 4.70 (s, 1H), 4.67 (s, 1H), 4.52 (s, 1H), 4.51 (s, 1H), 2.35 (s, 3H), 2.30 (s, 3H), 2.24 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.8, 144.7, 144.5, 143.3, 141.5, 140.7, 139.6, 138.3, 137.9, 135.2, 134.8, 133.2, 132.2, 131.7, 131.5, 130.6, 130.3, 129.6, 129.1, 128.9, 128.6, 128.4, 128.4, 127.6, 127.5, 127.4, 126.5, 126.4, 123.4, 122.4, 122.4, 121.8, 121.7, 121.5, 121.4, 121.2, 121.0, 120.8, 62.7, 62.4, 49.5, 49.4, 49.1, 49.0, 22.3, 22.0, 21.2, 20.9. ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{29}H_{23}NO_2SNa^+$ 472.1341, Found 472.1339.

Scale-up Experiment. To a solution of *N*-sulfonyl ketimine **1a** (1.0 g, 3.7 mmol), KF (1.1 g, 18.5 mmol), 18-crown-6 (4.9 g, 18.5 mmol) in anhydrous acetonitrile (25 mL) was added 2-(trimethylsilyl)-aryl triflate **2a** (2.8 mL, 11.1 mmol). The mixture was stirred for 6 h at room temperature under an argon atmosphere. Then mixture was diluted with CH_2Cl_2 (30 mL), filtered through a short pad of silica gel and the solvent was evaporated. Subsequently, the crude residue was purified by flash column chromatography on silica gel to afford pure **3a** in 80% yield (1.25 g), thus indicating that this transformation is easy to scale up to gram scale without loss of efficiency.

General Procedure for the IED aza Diels−Alder Reaction Involving N-Sulfonyl Ketimines and Arynes. To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the 18-crown-6 (132 mg, 0.50 mmol, 2.5 equiv) and KF (30 mg, 0.50 mmol, 2.5 equiv) under argon atmosphere, then *N*-sulfonyl ketimine **1** (0.20 mmol, 1.0 equiv) was added and the screw-capped tube was evacuated and backfilled with argon. The mixture was dissolved in CH_3CN (3.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at room temperature for 5 min. To the stirring solution was added *β*-trimethylsilyltriflate **1** (0.25 mmol, 1.25 equiv) dropwise, further allowed to stir for 6 h. Then mixture was diluted with CH_2Cl_2 (5.0 mL) and the solvent was evaporated. Subsequently, the crude residue was purified by flash column chromatography on silica gel to afford the corresponding isothiazole dioxide-fused dihydroquinoline derivatives **4a−4j** in good yields.

*5-Phenyl-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4a**).* White solid (0.047 g, 67% yield, mp 164.6−166.7 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3474, 3416, 1639, 1620, 1502, 1354, 1175, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.88 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.65−7.61 (m, 2H), 7.61−7.54 (m, 1H), 7.33−7.22 (m, 6H), 7.02 (d, J = 3.7 Hz, 2H), 5.75 (d, J = 4.3 Hz, 1H), 4.95 (d, J = 4.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.8, 133.3, 132.1, 131.3, 130.8, 130.2, 128.9, 128.4,

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128.3, 127.8, 127.6, 127.0, 124.8, 124.4, 121.0, 120.9, 115.1, 103.2, 43.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{21}H_{15}NO_2SNa^+$ 368.0716, Found 368.0713.

*5-(4-Methoxyphenyl)-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4b**).* Pale yellow gum (0.044 g, 58% yield); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3455, 1635, 1510, 1318, 1160, 808 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.6 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 3.0 Hz, 2H), 7.61−7.59 (m, 1H), 7.29−7.25 (m, 1H), 7.16 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 4.2 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.76 (d, J = 4.3 Hz, 1H), 4.93 (d, J = 4.2 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 158.6, 138.2, 133.3, 132.1, 131.2, 130.8, 130.1, 129.4, 128.4, 127.7, 127.5, 124.8, 121.1, 120.9, 115.1, 114.2, 103.4, 55.3, 42.4 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{22}H_{18}NO_3S^+$ 376.1002, Found 376.0998.

*5-(4-Isopropylphenyl)-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4c**).* Colorless solid (0.048 g, 62% yield, mp 101.1−103.2 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3455, 1633, 1462, 1179, 1022, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 3.3 Hz, 2H), 7.61−7.59 (m, 1H), 7.30−7.27 (m, 2H), 7.17 (s, 3H), 7.05 (d, J = 5.8 Hz, 2H), 5.79 (d, J = 4.3 Hz, 1H), 4.97 (d, J = 4.3 Hz, 1H), 2.87 (dd, J = 13.8, 6.9 Hz, 1H), 1.22 (d, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 147.7, 143.2, 133.3, 130.8, 130.1, 128.4, 128.3, 127.8, 127.6, 126.9, 124.7, 124.6, 121.1, 120.9, 115.1, 103.5, 42.9, 33.7, 23.9 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{24}H_{22}NO_2S^+$ 388.1366, Found 388.1373.

*5-(4-Fluorophenyl)-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4d**).* Pale yellow solid (0.044 g, 61% yield, mp 118.7−120.1 °C); R_f = 0.4 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3461, 3420, 1637, 1505, 1349, 1272, 870 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.91 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.68 (d, J = 2.9 Hz, 2H), 7.65−7.60 (m, 1H), 7.30 (d, J = 7.1 Hz, 1H), 7.21 (dd, J = 8.2, 5.5 Hz, 2H), 7.08−6.98 (m, 4H), 5.74 (d, J = 4.3 Hz, 1H), 4.99 (d, J = 4.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.8 (d, $^1J_{C-F}$ = 246.0 Hz), 141.5, 133.4, 132.2, 131.3, 130.7, 130.3, 129.8 (d, $^3J_{C-F}$ = 8.1 Hz), 128.2, 127.9, 127.8, 124.9, 124.2, 121.8, 120.9, 115.7 (d, $^2J_{C-F}$ = 21.4 Hz), 115.3, 109.7, 102.8, 42.5 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{21}H_{15}FNO_2S^+$ 364.0802, Found 364.0803.

*5-(m-Tolyl)-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4e**).* White solid (0.046 g, 64% yield, mp 159.3−161.7 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3452, 1632, 1455, 1381, 1050, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 3.4 Hz, 2H), 7.62−7.59 (m, 1H), 7.30−7.28 (m, 1H), 7.21 (t, J = 7.7 Hz, 1H), 7.05 (t, J = 5.8 Hz, 5H), 5.77 (d, J = 4.3 Hz, 1H), 4.95 (d, J = 4.2 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.7, 138.7, 133.3, 132.2, 131.3, 130.8, 130.2, 129.1, 128.8, 128.4, 127.9, 127.8, 127.6, 125.5, 124.8, 124.4, 121.1, 120.9, 115.2, 103.3, 43.2, 21.4 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{22}H_{18}NO_2S^+$ 360.1053, Found 360.1048.

*5-(3-Methoxyphenyl)-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4f**).* Pale yellow gum (0.042 g, 56% yield); R_f = 0.6 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3473, 3421, 1632, 1490, 1177, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.66 (t, J = 6.5 Hz, 2H), 7.64−7.61 (m, 1H), 7.28−7.22 (m, 2H), 7.05 (s, 2H), 6.84 (d, J = 7.5 Hz, 1H), 6.79 (s, 2H), 5.77 (d, J = 4.1 Hz, 1H), 4.96 (d, J = 3.9 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.0, 147.3, 133.3, 132.2, 131.3, 130.7, 130.2, 129.9, 128.3, 127.9, 127.8, 124.8, 124.2, 121.1, 120.9, 120.8, 115.2, 114.3, 112.1, 103.0, 55.2, 43.3 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{22}H_{17}NO_3SNa^+$ 398.0821, Found 398.0825.

*2,3-Dimethyl-5-phenyl-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4g**).* White solid (0.047 g, 63% yield, mp 176.8−179.7 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3473, 3417, 1620, 1377, 1174, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 3.8 Hz, 2H), 7.59 (dd, J = 7.4, 3.5 Hz, 2H), 7.33−7.309 (m, 2H), 7.26−7.23 (m, 3H), 6.77 (s, 1H), 5.74 (d, J = 4.3 Hz, 1H), 4.91 (d, J = 4.2 Hz, 1H), 2.28 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.1, 136.5, 133.3, 133.2, 132.3, 131.4, 130.0, 129.0, 128.9, 128.5, 128.3, 127.7, 126.9, 121.6, 121.1, 120.9, 115.9, 103.3, 42.9, 19.8, 19.2 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{23}H_{19}NO_2SNa^+$ 396.1029, Found 396.1035.

*2,3-Dimethoxy-5-phenyl-5H-benzo[4,5]isothiazolo[2,3-a]-quinoline 11,11-Dioxide (**4h**).* White solid (0.048 g, 59% yield, mp 155.3−158.7 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 1:1); IR (film) ν_{max} 3474, 3416, 1639, 1316, 1244, 1014 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.89 (d, J = 7.5 Hz, 1H), 7.65 (t, J = 6.6 Hz, 2H), 7.61 (dd, J = 8.4, 4.5 Hz, 1H), 7.38 (s, 1H), 7.34−7.31 (m, 2H), 7.26−7.23 (m, 3H), 6.47 (s, 1H), 5.74 (d, J = 4.1 Hz, 1H), 4.93 (d, J = 4.0 Hz, 1H), 3.97 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 148.5, 146.3, 145.7, 133.3, 132.2, 130.1, 128.9, 128.6, 128.2, 127.6, 127.1, 124.9, 121.1, 120.9, 115.9, 112.9, 103.1, 99.3, 56.1, 43.3 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{23}H_{19}NO_4SNa^+$ 428.0927, Found 428.0933.

*5-Phenyl-tetrahydrobenzo[4,5]isothiazolo[2,3-a]cyclopenta[g]-quinoline 11,11-Dioxide (**4i**).* Colorless solid (0.045 g, 59% yield, mp 188.1−191.3 °C); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3544, 3416, 1619, 1492, 1352, 1172, 804 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.90 (d, J = 7.6 Hz, 1H), 7.70 (s, 1H), 7.65 (d, J = 3.1 Hz, 2H), 7.61−7.57 (m, 1H), 7.34−7.30 (m, 2H), 7.26−7.21 (m, 3H), 6.87 (s, 1H), 5.75 (d, J = 4.2 Hz, 1H), 4.94 (d, J = 4.2 Hz, 1H), 2.94 (dd, J = 12.0, 7.1 Hz, 2H), 2.75 (dd, J = 13.0, 6.9 Hz, 2H), 2.07−1.99 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.2, 144.3, 140.9, 133.2, 132.3, 130.0, 129.5, 129.3, 128.9, 128.5, 128.4, 127.7, 126.9, 126.2, 122.2, 121.1, 120.9, 111.1, 103.2, 43.6, 32.9, 32.3, 25.5 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{24}H_{20}NO_2S^+$ 386.1209, Found 386.1216

*3-Methyl-5-phenyl-5H-benzo[4,5]isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4j**) and 2-Methyl-5-phenyl-5H-benzo[4,5]-isothiazolo[2,3-a]quinoline 11,11-Dioxide (**4j'**).* Pale yellow gum (0.045 g, 62% yield (inseparable mixture of isomers with a ratio of 2:1, determined by ^1H NMR)); R_f = 0.5 (silica, CH_2Cl_2:hexanes, 2:3); IR (film) ν_{max} 3464, 3424, 1636, 1632, 1293, 1026, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.91- 7.63 (m, 6H), 7.31- 7.23 (m, 5H), 6.88 (dd, J = 24.5, 9.1 Hz, 2H), 5.77 (d, J = 4.1 Hz, 1H), 4.95 (s, 1H), 2.37-2.21 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 145.9, 145.9, 137.9, 136.7, 134.4, 133.3, 133.3, 132.6, 132.5, 132.3, 132.2, 131.9, 131.2, 131.1, 130.7, 130.6, 130.1, 129.8, 129.4, 129.3, 128.9, 128.9, 128.6, 128.5, 128.4, 128.4, 128.3, 127.7, 126.9, 126.6, 125.8, 125.6, 124.2, 122.9, 122.0, 121.6, 121.5, 121.1, 120.9, 120.8, 115.5, 115.1, 103.4, 103.1, 43.3, 43.0, 21.4, 20.8 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{22}H_{18}NO_2S^+$ 360.1053, Found 360.1050.

Control Experiment. To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added the 18-crown-6 (131 mg, 0.5 mmol, 2.5 equiv) and KF (30 mg, 0.5 mmol, 2.5 equiv) under argon atmosphere, then dihydroquinoline **4a** (0.20 mmol, 1.0 equiv) was added and the screw-capped tube was evacuated and backfilled with argon. The mixture was dissolved in CH_3CN (3.0 mL) under argon atmosphere. The resultant reaction mixture was kept stirring at room temperature for 5 min. To the stirring solution was added β-trimethylsilyltriflate **1a** (75 mg, 0.25 mmol, 1.25 equiv) dropwise, further allowed to stir for 4 h. Then mixture was diluted with CH_2Cl_2 (5.0 mL) and the solvent was evaporated. Subsequently, the crude residue was purified by flash column chromatography on silica gel to afford dihydrocyclobutaquinoline **3a** in 93% yield.

This result confirms the stepwise ADAR followed by stereoselective [2+2] cycloaddition process in the synthesis of dihydrocyclobutaquinoline **3** from cyclic-1-azadienes **1**.

General Procedure for the Synthesis of 2,4-Diarylquinolines. Sodium hydroxide (12 mg, 0.30 mmol, 3.0 equiv) was added to dihydroquinoline **4** (0.10 mmol, 1.0 equiv) dissolved in CH_3OH (2.0 mL) and refluxed for 14 h. After completion of the reaction, as indicated by TLC, reaction mixture was diluted with ethyl acetate and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel to afford the corresponding 2,4-diarylquinoline derivatives in excellent yields.

*2,4-Diphenylquinoline (**5a**).*[22] Colorless solid (0.024 g, 86% yield, mp 111.4−113.6 °C); R_f = 0.6 (silica, ethyl acetate:hexanes, 1:4); IR (film) ν_{max} 3473, 3417, 1638, 1619, 792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.25 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 7.3 Hz, 2H), 7.91 (d,

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J = 8.3 Hz, 1H), 7.82 (s, 1H), 7.74 (t, J = 7.4 Hz, 1H), 7.57−7.47 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.9, 149.1, 148.8, 139.6, 138.4, 130.1, 129.5, 129.5, 129.3, 128.8, 128.6, 128.4, 127.6, 126.3, 125.7, 125.6, 119.3 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{21}H_{16}N^+$ 282.1277, Found 282.1282.

*4-(4-Isopropylphenyl)-2-phenylquinoline (**5c**).* Colorless gum (0.029 g, 89% yield); R_f = 0.6 (silica, ethyl acetate:hexanes, 1:4); IR (film) ν_{max} 3472, 3417, 1637, 1619, 1020, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, J = 8.4 Hz, 1H), 8.20−8.18 (m, 2H), 7.97 (d, J = 8.4 Hz, 1H), 7.82 (s, 1H), 7.75−7.73 (m, 1H), 7.56−7.38 (m, 8H), 3.04 (dt, J = 13.8, 6.9 Hz, 1H), 1.36 (d, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.9, 149.2, 148.8, 139.7, 135.8, 130.0, 129.5, 129.4, 129.2, 128.8, 127.6, 126.6, 126.2, 125.8, 125.8, 119.4, 33.9, 24.0 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{24}H_{22}N^+$ 324.1747, Found 324.1739.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02667.

Spectral data for all compounds and X-ray data for **3a** (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: wangz1114@cqu.edu.cn
*E-mail: yun.he@cqu.edu.cn

ORCID

Yun He: 0000-0002-5322-7300

Author Contributions

†I.N.C.K. and R.S.R. contributed equally

Notes

The authors declare no competing financial interest.

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