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A Palladium-Catalyzed Method for the Synthesis of 2-(α-Styryl)-2,3-dihydroquinazolin-4-ones and 3-(α-Styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxide: Access to 2-(α-Styryl)quinazolin-4(3*H*)-ones and 3-(α-Styryl)-1,2,4-benzothiadiazine-1,1-dioxides

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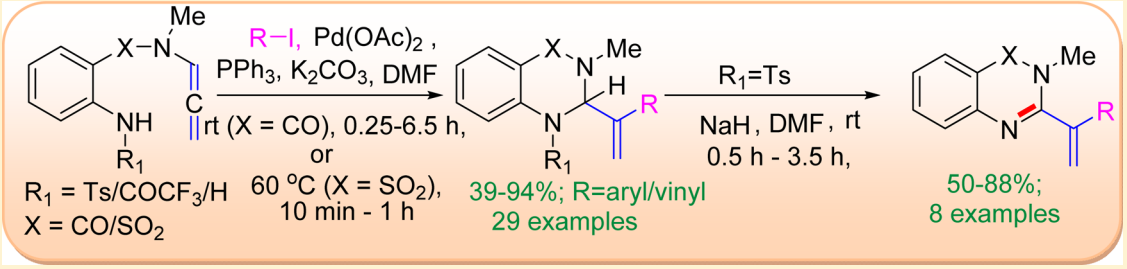
Supporting Information



ABSTRACT: An efficient synthesis of 2-(α-styryl)-2,3-dihydroquinazolin-4-ones and 3-(α-styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxides has been achieved in 39−94% yield through palladium-catalyzed cyclocondensation of aryl/vinyl iodides with allenamides **13**−**15** and **22**, respectively. Base treatment of the *N*-tosylated products provides an easy access to 2-(α-styryl)quinazolin-4(3*H*)-ones and 3-(α-styryl)-1,2,4-benzothiadiazine-1,1-dioxides, hitherto unknown heterocycles. The method has been tested with phenyl substituted allenamides, applied for bis-heteroannulation, and used in the preparation of analogues of the natural product *Luotonin F*.

INTRODUCTION

Quinazolin-4(3*H*)-one (**1a**, Figure 1) constitutes an important class of heterocycles being an integral part of a large number of naturally occurring alkaloids (∼150) and drug candidates.[1] It exhibits a broad range of biological activities such as anticancer,[2a,b] antiviral,[2c] antimalarial,[2d] antifungal,[2e] and human microsomal prostaglandin synthase 1 (mPGES-1) inhibitor.[2f] The 2-styryl derivatives are considered as privileged structures in medicinal chemistry because of their promising pharmacological effects. For example, compounds of type **2** (Figure 1) exhibit significant cytotoxicity in L1210 murine leukemia cells and inhibitory effects on tubulin polymerizations,[3] while CP-465,022 (**3**, Figure 1) is recognized as a noncompetitive antagonist of AMPA-selective glutamate receptors.[4] Very recently, compound **4a** was discovered as a potent antibiotic by high throughput virtual screening of a large number of compounds; further optimization by screening studies of analogues led to the development of an even better candidate **4b**, which showed remarkable *in vitro* and *in vivo* (methicillin-resistant *Staphylococus aureus* mouse model) efficacy with improved pharmacokinetics.[5]

On the other hand, 1,2,4-benzothiadiazine-1,1-dioxides **1b** form another class of remarkably important heterocycles because of their wide range of activities such as antihypertensive,[6a] antiviral,[6b] antimicrobial,[6c] and ATP sensitive potassium channel opener,[6d] among others, and their uses in the development of therapeutics. For example, compound **5** has shown promising activity in the area of diabetes and obesity being a potent HCV NS5B polymerase inhibitor,[7] while Diazoxide (compound **6**, Figure 1) is a K^+[ATP] channel agonist and has a beneficial effect in obese hyperinsulinemic adults.[8]

Though a number of methods using either conventional reagents[9,10] or transition metal catalysts[11,12] are known for the synthesis of **1a** and **1b**, only a limited number,[13] which mainly rely on acid-[13a,b,d,e] or base[13f]-promoted Knoevenagel condensation of 2-methyl quinazolinones with aromatic/heteroaromatic aldehydes, exist for the synthesis of 2-β-styryl derivatives of quinazolin-4(3*H*)-ones (e.g., **2**, **4**). On the other hand, the synthetic methods available for 2-β-styryl derivatives of benzothiadiazine-1,1-dioxide are rare.[14] To the best of our knowledge, there is no reported synthesis of 2-(α-styryl)quinazolin-4(3*H*)-ones **7** (a regioisomer of the β-styryl counterpart) and their benzothiadiazine-1,1-dioxide analogues **8**, which could serve as important pharmacophores in drug discovery. This prompted us to establish convenient methods for their general synthesis. Following our efforts[15] to identify

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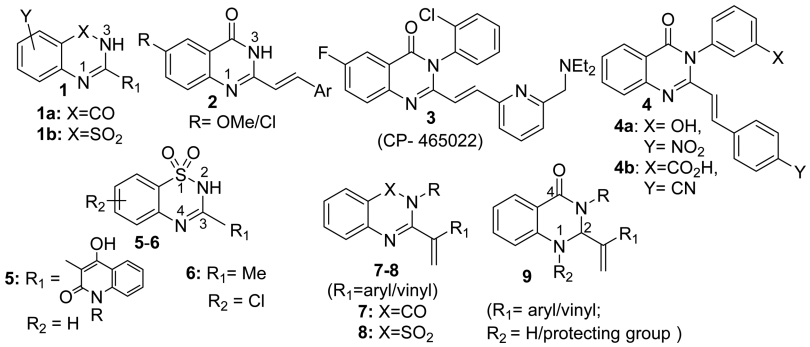
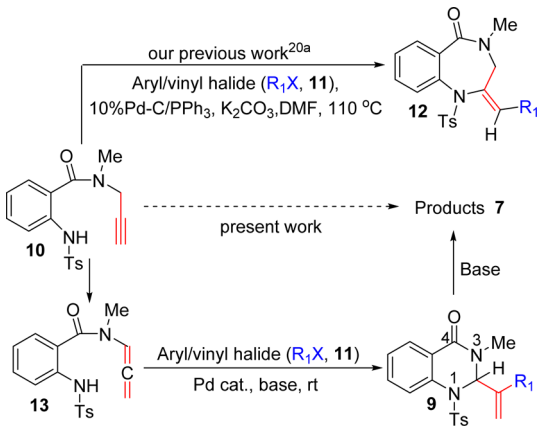


Figure 1. General structures of quinazolin-4(3*H*)-ones, 1,2,4-benzothiadiazine-1,1-dioxides, and their 2-*β*-styryl derivatives, and examples of biologically active compounds belonging to these classes.

lead compounds having significant anticancer properties, we also became interested to get access to the scaffolds **7** and **8**, which could enable us to explore their potency in cancer therapy.

Previous workers reported the synthesis of the N^3-alkylated derivatives of **1a** through oxidation of 2,3-dihydroquinazolin-4(1*H*)-ones using conventional oxidants [e.g., DDQ,[16a] $KMnO_4$,[16b] MnO_2,[16c] I_2[16d]] or metal catalysts.[16e,f] Therefore, we assumed that the synthesis of **7** could also be achieved easily by oxidizing the corresponding dihydro analogues **9** (Figure 1, R_2 = H). Scrutiny of the literature revealed only one earlier example, that of Broggini et al.[17] for the synthesis of *N*-Boc-2-*α*-styryl-1,2-dihydroquinazolin-4-ones **9** (R_2 = Boc). However, Boc deprotection of the reported compound **9** (R_2 = Boc, R_1 = Ph, R = Me), followed by oxidation of the resulting product using conventional oxidants,[16a−d] delivered only a trace amount of **7** (R_1 = Ph, R = Me) in a few cases. This prompted us to conceive a novel strategy for the synthesis through a base-promoted reaction on **9** containing acidic aminal hydrogen (at C2). However, application of this strategy on **9** (R_2 = Boc, R_1 = Ph, R = Me) employing various bases failed to deliver any product. As N-tosylated heterocycles have been reported[18] to undergo elimination of the protecting group (i.e., Ts) under basic conditions along with a neighboring proton to generate a double bond, we chose the sulphonyl moiety as an alternative N-protecting agent to establish a viable synthesis of **7** (Scheme 1). Thus, we needed to synthesize *N*-sulphonyl derivatives of **9** (R_2 = SO_2R) as precursors, which are unknown in the literature.

Scheme 1. Our Previous Work and Envisaged Route for the Present Synthesis of 7



Encouraged by the recent spectacular advances in the area of palladium-catalyzed heteroannulations involving intramolecular nucleophilic attack of the nitrogen atom onto an allene moiety[19] and in continuation of our work[20] on the synthesis of novel heterocycles of biological interests, we envisioned that allenamide **13**, generated easily from the acetylenic substrate **10** which was used successfully in our previous synthesis[20a] of (*E*)-2-arylmethylidene-1,4-benzodiazepinones **12**, could undergo reaction with aryl/vinyl halides **11** under palladium catalysis, affording the requisite *N*-tosyl-2,3-dihydroquinazolin-4-one **9** (Scheme 1). Our hypothesis indeed proved to be viable after choosing an appropriate catalyst and a suitable base. We then expanded the scope of this reaction to 1,2,4-benzothiadiazine-1,1-dioxides as well. In a subsequent step, we also realized the convenient synthesis of products **9** employing a suitable base. Herein, we describe the results obtained so far in detail.

RESULTS AND DISCUSSION

Synthesis of anthranilic allenamide **13**, the requisite starting substrate, was achieved (with 85% yield) easily upon base treatment of the *N*-propargylated anthranilamide **10**. Thereafter, we attempted the synthesis of *N*-sulphonyl-2-*α*-styryl-2,3-dihydroquinazolin-4-ones **9** at room temperature through palladium-catalyzed reactions. Initially, carrying out the reaction of **13** with phenyl iodide (**11a**) employing the catalyst, solvent, and base used by Broggini et al.[17] required 14 h to produce the desired product **9aa** (75% yield), thereby marking the process as sluggish (Table 1, entry 1). In order to find the optimal reaction conditions, we performed a series of reactions on the model substrates **11a** and **13** by changing catalyst, base, solvent, etc.; selected results are summarized in Table 1. Employment of our recently reported[20a] catalytic system [Pd/C, PPh_3, K_2CO_3, DMF] in this reaction required even more time (26 h) to complete this reaction at rt (Table 1, entry 2 vs 1). Interestingly, replacing the catalyst by $Pd(dba)_2$ reduced the reaction time (15 h) and improved the yield (90%) significantly (Table 1, entry 3). To our disappointment, switching to a more polar solvent like DMSO proved to be ineffective, decreasing the yield to 50% even after increasing the reaction time to 60 h (Table 1, entry 4), while an alkaline base (i.e., KOH) proved to be completely inefficient, showing no sign of product formation (Table 1, entry 5). We were encouraged to note that the use of $Pd(MeCN)_2Cl_2/PPh_3$ and K_2CO_3 in DMF produced the product **9aa** within 8 h, albeit in moderate (47%) yield (Table 1, entry 6). Gratifyingly, use of $Pd(OAc)_2$ allowed the reaction to be completed within 1 h at rt, affording product **9aa** in 94% yield (Table 1, entry 7). The use of other bases (e.g.,

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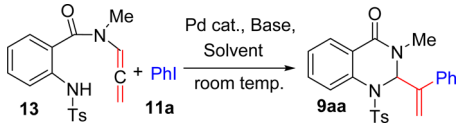
Table 1. Optimization of the Reaction Conditions for the Synthesis of 9aa at Room Temperature[a]



Sl. no.	cat.[b]	base	solvent	time (h)	yield (%)[c]
1	$Pd(PPh_3)_4$	K_2CO_3	CH_3CN	14	75
2	10% Pd/C	K_2CO_3	DMF	26	68
3	$Pd(dba)_2$	K_2CO_3	DMF	15	90
4	$Pd(dba)_2$	K_2CO_3	DMSO	60	50
5	$Pd(dba)_2$	KOH	DMF	2	0
6	$Pd(MeCN)_2Cl_2$	K_2CO_3	DMF	8	47
7	**$Pd(OAc)_2$**	**K_2CO_3**	**DMF**	**1**	**94**
8	$Pd(OAc)_2$	KO^{t}Bu	DMF	1	91
9	$Pd(OAc)_2$	Cs_2CO_3	DMF	4	82
10	$Pd(OAc)_2$	Et_3N	DMF	2.5	88
11	$Pd(PPh_3)_2Cl_2$	K_2CO_3	DMF	30	65

[a]Reaction conditions: **13** (1.0 equiv), **11a** (1.0 equiv), palladium catalyst (0.05 equiv), PPh_3 (0.12 equiv, except for entry 1), base (4.0 equiv) in a solvent under argon. [b]PPh_3 was used as ligand except for entry 1. [c]Yields of isolated pure products.

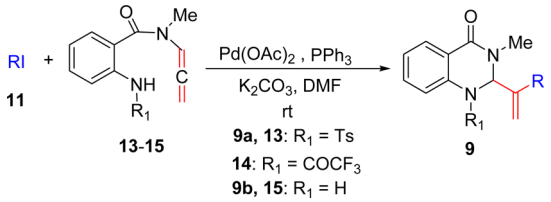
KO^{t}Bu, Cs_2CO_3, Et_3N) neither improved the yield nor reduced the reaction time (Table 1, entries 8–10). Additionally, $Pd(PPh_3)_2Cl_2$ proved unsuitable (Table 1, entry 11). DMF was found to be the best solvent. Thus, the reaction conditions of entry 7 of Table 1 appeared to be optimal.

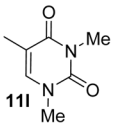
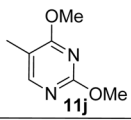
Using the optimized reaction conditions, we then extended the scope of this procedure to anthranilic allenamides **13–15** and a range aryl/heteroaryl/vinyl iodides **11a–l** (Table 2). Indeed, allenamide **13** reacted successfully with a series of iodides **11a–l**, furnishing the expected products **9aa–al** with moderate to excellent yields (Table 2, entries 1–12). Heteroaryl iodides without any substitution (**11b,c**) also produced desired products **9ab–ac**, though with somewhat lower yields (66–73%) compared to phenyl iodide (**11a**), proving their lower reactivity in this reaction (Table 2, entries 2–3 vs entry 1). An electron-donating group enhanced the reactivity (in **11j**), delivering product **9aj** with 89% yield (Table 2, entry 10). On the other hand, irrespective of the substitution, all aryl iodides **11d–i** possessing either electron-donating (viz., Me, OMe) or electron-withdrawing groups (viz., CF_3, CHO, CO_2Me, NO_2) efficiently participated in this reaction to produce the products (**9ad–ai**) within 2.5 h with 66–86% yields (Table 2, entries 4–9). Additionally, olefinic iodides were found to be reactive under the conditions (Table 2, entries 11 and 12). Though vinyl iodide **11k** furnished the product **9ak** with moderate yield (39%), 2,4-dimethyl-5-iodo-uracil (**11l**) afforded the desired compound **9al** with 63% yield. Unfortunately, neither any aryl bromide/chloride nor allenamide without *N*-alkylation (of the amidic nitrogen) reacted.

To check the effect of other N-protecting groups, the reactivity of trifluoroacetanilide substituted allenamide **14** toward different aryl iodides was explored (Table 2, entries 13–16). Interestingly, this gave direct access to the N-deprotected products (Table 2, entries 13–16), which is similar to the observations of Cacchi and co-workers.[21] Furthermore, the presence of an electron-withdrawing group in the iodide facilitated the reaction compared to an electron-donating group (Table 2, entry 16 vs 15).

Encouraged by these results, we became interested to test allenamide **15**, which has a free amine group, in this reaction. Interestingly, this too resulted in the formation of the desired products with moderate to good yields (Table 2, entries 17–

Table 2. Palladium-Catalyzed Synthesis of 2-(α-Styryl)-2,3-dihydroquinazolin-4-ones 9[a]



Entry	Allenamide	RI (**11**) R	Time (h)	Product	Yield (%)[b]	Entry	Allenamide	RI (**11**) R	Time (h)	Product	Yield (%)[b]
1	**13**	Ph; **11a**	1	**9aa**	94	11	**13**	vinyl; **11k**	1.5	**9ak**	39
2	**13**	3-pyridyl; **11b**	0.5	**9ab**	73	12	**13**		0.75	**9al**	63
3	**13**	2-thienyl; **11c**	0.75	**9ac**	66						
4	**13**	C_6H_4Me-*p*;**11d**	0.25	**9ad**	73						
5	**13**	$C_6H_4CF_3$-*p*; **11e**	2	**9ae**	74						
6	**13**	C_6H_4OMe-*p*; **11f**	0.5	**9af**	74	13	**14**	**11a**	0.75	**9ba**	74
7	**13**	$C_6H_4CO_2$Me-*p*; **11g**	2.5	**9ag**	86	14	**14**	**11e**	2	**9bb**	58
8	**13**	C_6H_4CHO-*o*; **11h**	0.5	**9ah**	75	15	**14**	**11f**	1.5	**9bc**	50
9	**13**	$C_6H_4NO_2$-*p*; **11i**	1	**9ai**	66	16	**14**	**11g**	1.5	**9bd**	83
						17	**15**	**11a**	0.75	**9ba**	60
10	**13**		4	**9aj**	89	18	**15**	**11f**	1.5	**9bc**	49
						19	**15**	**11g**	1.5	**9bd**	80
						20	**15**	**11j**	6.5	**9be**	55

[a]Reaction conditions: **13/14/15** (1.0 equiv), **11** (1.0 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.12 equiv), K_2CO_3 (4.0 equiv) in DMF under argon. [b]Yield of isolated pure product.

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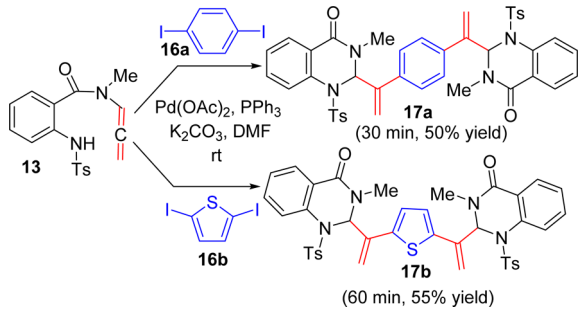
20). However, in line with our previous observation, an iodide possessing an electron-withdrawing group (e.g., CO_2Me) turned out to be more reactive compared to one having an electron-donating group like OMe (Table 2, entry 19 vs 18, 20). From these studies, it is apparent that allenamide **13** containing the *N*-tosyl group possessed better reactivity than other allenamides (**14**, **15**) and delivered the products with very good yields. This underlines the crucial role of the acidic hydrogen attached to the aryl amino moiety (in allenamide), acting as a nucleophile during cyclization.

Bis-heteroannulated products **17a** and **17b** could also be accessed easily, though in moderate yields, when allenamide **13** was allowed to react with aryl diiodides **16a** and **16b** under the optimized reaction conditions, suggesting polyheteroannulation to be a viable process in one pot (Scheme 2).

Scheme 2. Synthesis of Bis-heteroannulated Products 17a–b[a]

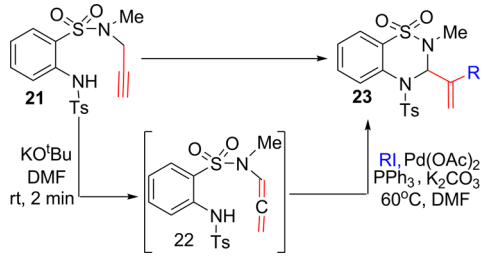


[a]Reaction conditions: **13** (1.0 equiv), **16a**/**16b** (0.5 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.12 equiv), K_2CO_3 (4.0 equiv) in DMF under argon.

To check the scope of this method further, an internal alkyne **18** was probed. It was surprising to find that even phenyl substituted crude allenamide **19** (having a propensity toward decomposition during purification through silica-gel column chromatography) reacted successfully with iodo compound **11g** under the optimized reaction conditions to furnish the stereoselective product **20** in 55% yield (Scheme 3). The (*E*)-stereochemistry of the product was confirmed by 2D NMR. Of particular interest was the weak, but perceptible, NOE cross peaks observed between the signals for the ortho protons (with respect to the olefinic double bond, as marked with green arrow) of the two phenyl rings of the styryl unit which established the geometry shown (see the Supporting Information).

After having accomplished a general synthesis of 2-(α-styryl)-2,3-dihydroquinazolin-4-ones **9**, we planned to replace the carbonyl (CO) group of allenamide **13** by a SO_2 group and used the allenesulfonamide derivative **22** for the synthesis of 3-(α-styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxide **23**. An initial base (KO^tBu)-promoted isomerization of the precursor acetylene compound (**21**) furnished the desired allenesulfonamide **22**. Since this compound was found to decompose during chromatographic purifications, we directly exposed the crude allenesulfonamide (obtained after usual workup) to react with phenyl iodide (**11a**) and 3-iodo-pyridine (**11b**) separately under optimized reaction conditions; to our disappointment, conducting these reactions at rt required 30 and 45 h, respectively, to deliver the corresponding products **23a** (47%) and **23b** (55%), proving them inconvenient to pursue. Pleasingly, the reactions were found to be completed within 25–30 min upon heating at 60 °C, and the yield improved as well (Table 3, entries 1 and 2). Furthermore, a

Table 3. Palladium-Catalyzed Synthesis of 3-(α-Styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxide 23[a,b]



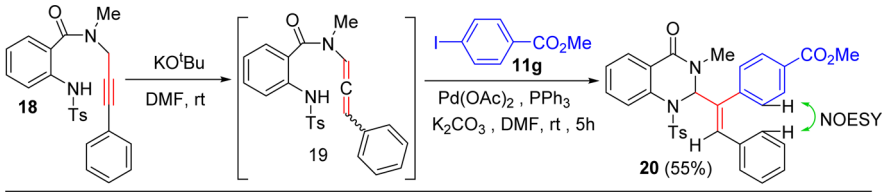
SI. No.	RI (11)	time (min)	product	yield (%)[c]
1	**11a**	30	**23a**	67
2	**11b**	25	**23b**	62
3	**11c**	30	**23c**	40
4	**11d**	15	**23d**	63
5	**11e**	10	**23e**	88
6	**11f**	60	**23f**	39
7	**11g**	30	**23g**	52
8	IC_6H_4F-*p*; **11m**	15	**23m**	63
9	IC_6H_4Br-*p*; **11n**	10	**23n**	61

[a]Reaction conditions: **21** (1.0 equiv), KO^tBu (2.0 equiv) in DMF. [b]Reaction conditions: Crude **22** treated with **11** (1.0 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.12 equiv), and K_2CO_3 (4.0 equiv) in DMF under argon. [c]Yield was calculated based on **21**.

heteroaryl iodide (Table 3, entry 3) and aryl iodides containing either electron-donating (Table 3, entries 4, 6) or electron-withdrawing (Table 3, entries 5, 7, 8, 9) groups underwent reaction successfully with crude allenesulfonamide **22** within 10–60 min to afford the expected products in moderate to very good yields (39–88%).

The structures of the products[23] were unambiguously deduced from spectroscopic (^1H, ^{13}C NMR, HRMS) and

Scheme 3. Reaction of Phenyl Substituted Allenamide 19 with Iodo Compound 11g[a,b]



[a]Reaction conditions: KO^tBu (2.0 equiv), in DMF at rt under an argon atmosphere. [b]Reaction conditions: Crude **19** treated with **11g** (1.0 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.12 equiv), and K_2CO_3 (4.0 equiv) in DMF under argon.

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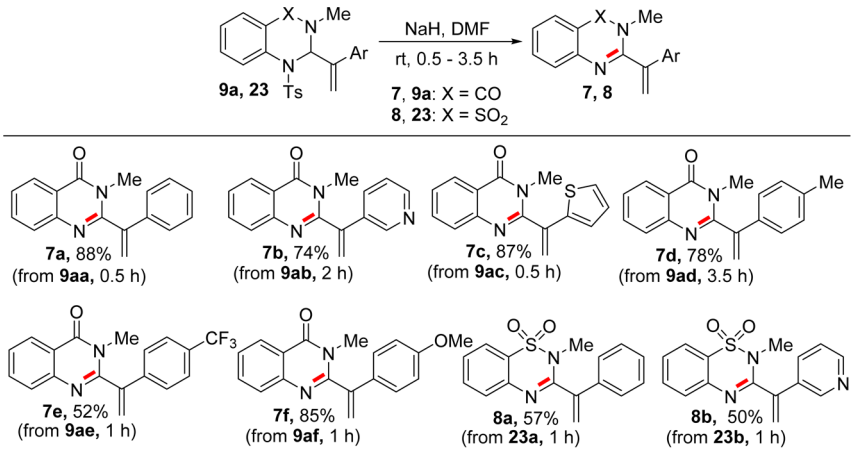
Scheme 4. Base-Promoted Synthesis of Products 7, 8[a,b]

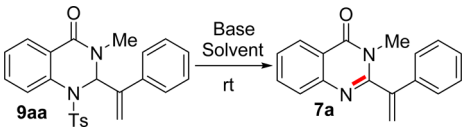


[a]Reaction conditions: For substrate **9a** (1.0 equiv), 5.0 equiv of NaH (60% dispersion in mineral oil) used; for substrate **23** (1.0 equiv), 2.0 equiv of the same base used, as excess base (5.0 equiv) was detrimental for yields. [b]Yield of isolated pure product.

analytical data. These were further supported by single crystal X-ray diffraction analysis (see the Supporting Information) of a few products (**9aa**, **9bd**, and **23g**).[22]

After achieving the synthesis of 2-(α-styryl)-2,3-dihydroquinazolin-4-ones **9** and their benzothiadiazine-1,1-dioxide variants **23**, attention was turned toward the synthesis of the unsaturated analogues **7** through a base-promoted reaction as depicted in Scheme 4. Initially, we performed a series of reactions on model compound **13a** varying the base and solvent as well; representative data are shown in Table 4. KO^{t}Bu-promoted reaction in THF at rt remained mostly incomplete (TLC), even after extending the reaction to 30 h, and yielded only 28% of the desired product **7a** along with the recovery (58%) of the reactant **9aa** (Table 4, entry 1). Gratifyingly, the reaction was complete within 5 min on replacing the solvent by DMF and the yield also improved somewhat (40%), though several side products (TLC) were generated (Table 4, entry 2). Thereafter, the use of KOH instead of KO^{t}Bu increased the yield to 60% (Table 4, entry 3), but the product **7a** was still accompanied by side products (TLC) in minor amounts. Though a strong organic base like DBU proved to be ineffective for this reaction (Table 4, entry 4), the use of NaH (5 equiv) was beneficial, leading to the formation of **7a** (88% yield) within 30 min (Table 4, entry 5); however, decreasing the amount of NaH (3 equiv) caused incomplete conversion of starting material even after 48 h. Further, changing the solvent to acetonitrile was not useful (Table 4, entry 6). Thus, reaction conditions of entry 5 in Table 4 proved optimal. We then checked the scope and limitations of this protocol by varying the substrates as shown in Scheme 4.

Table 4. Optimization of the Reaction Conditions for the Synthesis of 2-(α-Styryl)quinazolin-4(3*H*)-one 7a



entry	base	solvent	time	yield[c] (%)
1[a]	KO^{t}Bu	THF	30 h	28
2[a]	KO^{t}Bu	DMF	5 min	40
3[a]	KOH	DMF	5 min	60
4[a]	DBU	DMF	38 h	0
5[b]	NaH	DMF	30 min	88
6[b]	NaH	CH_3CN	38 h	60

[a]Reaction conditions: **9aa** (1.0 equiv), base (3.0 equiv). [b]Reaction conditions: **9aa** (1.0 equiv), NaH (60% dispersion in mineral oil, 5.0 equiv). [c]Yield of isolated pure product.

As depicted in Scheme 4, substrates **9aa**−**9ac** containing a simple aryl/heteroaryl group in the styryl moiety afforded products (**7a**−**c**) in very good yield (74−88%). Even after introduction of an electron-donating group (viz. Me/OMe) in the aryl ring (substrates **9ad**/**9af**), the corresponding products **7d**/**7f** were isolated with comparable yields (78−85%). In contrast, an electron-withdrawing substituent (viz. CF_3) at the same position of the substrate (**9ae**) reduced the yield (52%) of the product (**7e**). On the other hand, employing substrates **23a** and **23b** having a SO_2 moiety in place of carbonyl delivered the desired products **8a** and **8b**, respectively, in moderate yield (57% and 50%).

The structures of the products were confirmed by spectroscopic analysis (^{1}H NMR, ^{13}C NMR, HRMS) and further supported by single crystal X-ray diffraction of compound **7d** (see the SI).[22]

We next applied this methodology for synthesizing (Scheme 5) analogues of *Luotonin F*,[24] a natural alkaloid extracted from the aerial parts of *Peganum nigellastrum* Bunge, the plant which finds applications in the Chinese system of medicines for the treatment of rheumatism, inflammation, abscesses, and other diseases.[25] The total synthesis of *Luotonin F* itself applying our methodology is presently underway.

CONCLUSION

In conclusion, we have successfully developed a facile and mild method for the general synthesis of 2-(α-styryl)-2,3-dihydroquinazolin-4-ones **9** via palladium-catalyzed cyclocondensation of aryl/heteroaryl (or vinyl) iodide **11** with allenamides **13**−**15** at room temperature. This reaction can easily be extended for bis-heteroannulation and the use of phenyl substituted allenamide as well. Besides, the scope of this method has been extended to the synthesis of 3-(α-styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxides **23** by varying the substrate (**22**) and tweaking the temperature (i.e., 60 °C). A base-

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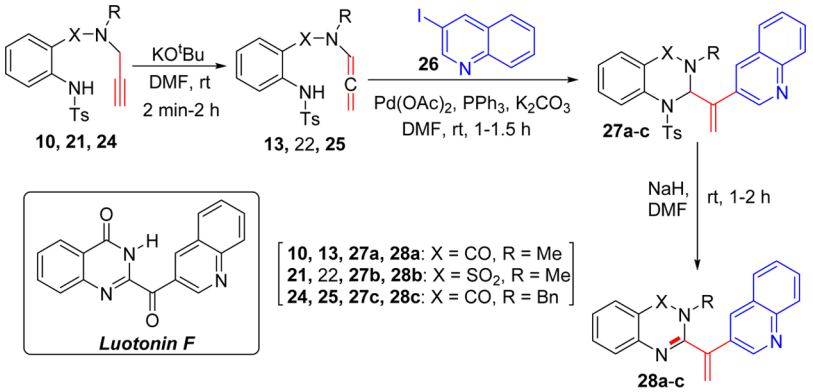
Scheme 5. Application of the Methodology for the Synthesis of *Luotonin F* Analogues[a,b,c]



[a]Reaction conditions: 2.0 equiv of KO^{t}Bu was used for **10**/**21** (1.0 equiv), but 3.0 equiv of the same base was used for **24** (1.0 equiv). [b]Reaction conditions: **13**/**25** (1.0 equiv), **26** (1.0 equiv), $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.12 equiv), K_2CO_3 (4.0 equiv). [c]For 1.0 equiv of **27a** and **27c**, 5.0 equiv of NaH (60% dispersion in mineral oil) was used; while, for **27b** (1.0 equiv), 2.0 equiv of the same base was used.

promoted reaction of the products (**9a**, **23**) provided an easy access to 2-(α-styryl)quinazolinones **7** and 3-(α-styryl)-1,2,4-benzothiadiazine-1,1-dioxide **8**, a novel class of compounds. This methodology has also been applied in the generation of a few analogues of *Luotonin F*. As 2-(β-styryl)quinazolinones have already proved to be potent inducers of apoptosis and possess other remarkable phamacological activities, their 2-(α-styryl) variants are also anticipated to possess potent medicinal value. Work in this direction is currently in progress and will be reported in due course.

EXPERIMENTAL SECTION

General. Melting points are uncorrected. Analytical thin-layer chromatography (TLC) was performed on Silica gel 60-F254 aluminum TLC sheets. Visualization of the developed chromatogram was performed by UV absorbance or iodine exposure. For purification, column chromatography was performed using 100−200 mesh silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 298 K on a 300, 400, 500, or 600 MHz spectrometer using tetramethylsilane (TMS) as internal standard. Chemical shifts (δ) are given from TMS (δ = 0.00) in parts per million (ppm) with reference to the residual nuclei of the deuterated solvent used [$CDCl_3$: ^{1}H NMR δ = 7.26 ppm (s); ^{13}C NMR δ = 77.0 ppm]. Coupling constants (J) are expressed in hertz (Hz), and spin multiplicities are given as s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), and br (broad). All ^{13}C NMR spectra were obtained with broad-band proton decoupling. To assign the structures under consideration, the following 1D and 2D experiments were employed: ^{1}H selective NOESY 2D: COSY and ^{1}H−^{13}C gradient selected HSQC and HMBC in a 600 MHz NMR machine. Mass spectra were performed using ESI-TOF, EI or FAB ionization mode.

Synthesis of Allenamides 13−15 from Corresponding Acetylene Compounds 10, S1, S2. *Synthesis of the Acetylenic Substrate N-Methyl-N-(prop-2-yn-1-yl)-2-(2,2,2-trifluoroacetamido)benzamide (**S1**).* The acetylene compounds 2-amino-*N*-methyl-*N*-(prop-2-yn-1-yl)benzamide (**S2**) and *N*-methyl-2-[(4-methylphenyl)sulfonamide]-*N*-(prop-2-yn-1-yl)benzamide (**10**) were prepared by a known literature procedure.[20a] *N*-Methyl-*N*-(prop-2-yn-1-yl)-2-(2,2,2-trifluoroacetamido)benzamide (**S1**) was prepared by adding trifluoroacetic anhydride (223 mg, 1.06 mmol) and triethylamine (81 mg, 0.80 mmol) in the solution of **S2** (100 mg, 0.53 mmol) in THF (5.0 mL) at 0 °C, followed by stirring at room temperature for 3 h. After completion of reaction (TLC), the solvent was evaporated *in vacuo*; the residue was washed with aqueous $NaHCO_3$ solution and partitioned between EtOAc and brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was then purified by silica gel (100−200 mesh) column chromatography using 12% ethyl acetate−petroleum ether (v/v) as eluent.

*N-Methyl-N-(prop-2-yn-1-yl)-2-(2,2,2-trifluoroacetamido)-benzamide (**S1**).* Pale yellow amorphous solid (130 mg, 86% yield); mp 90−92 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.32 (brs, 1H), 8.29 (d, J = 8.4 Hz, 1H), 7.54−7.48 (m, 2H), 7.28−7.23 (m, 1H), 4.25 (m, 2H), 3.18 (s, 3H), 2.37 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.7, 155.1 (q, J = 37.2 Hz), 134.8, 131.6, 127.9, 125.0, 124.0, 122.9, 115.6 (q, J = 286.7 Hz), 77.6, 73.4, 42.4, 36.9 ppm; HRMS (ESI$^+$) m/z calculated for $C_{13}H_{11}F_3N_2O_2Na$ $[M + Na]^+$ 307.0670, found 307.0672.

Procedure for Conversion of 10, S1, S2 to Allenamides 13, 14, 15. *N-Methyl-2-[(4-methylphenyl)sulfonamide]-N-(propa-1,2-dien-1-yl)benzamide (**13**).* To a stirred solution of acetylene **10** (100 mg, 0.29 mmol) in dry DMF was added KO^{t}Bu (66 mg, 0.58 mmol); the reaction was found to be completed within 5 min. (TLC). It was then quenched with water (5 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by silica gel (100−200 mesh) column chromatography using 20% EtOAc−petroleum ether (v/v) as eluent to furnish the product **13** as a white amorphous solid (85 mg, 85%); mp 108−109 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.41 (brs, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.55 (brs, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.21−7.12 (m, 4H), 5.98 (s, 1H), 5.45−5.35 (m, 2H), 2.97 (s, 2H), 2.47 (s, 1H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 201.3, 168.9, 145.6, 137.9, 137.7, 133.1, 131.0, 130.6, 129.4, 128.6, 127.2, 126.1, 104.5, 101.0, 88.9, 37.1, 32.9, 31.2, 23.0 ppm. HRMS (EI$^+$) m/z calculated for $C_{18}H_{18}N_2O_3S$ $[M]^+$ 342.1038, found 342.1034.

*N-Methyl-N-(propa-1,2-dien-1-yl)-2-(2,2,2-trifluoroacetamido)-benzamide (**14**).* To a well-stirred solution of acetylene **S1** (100 mg, 0.35 mmol) in dry DMF was added KO^{t}Bu (316 mg, 2.82 mmol), and the reaction was continued for another 10 min until completion (TLC). Then, the reaction was quenched with water (5 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*; the resulting residue was purified by silica gel (100−200 mesh) column chromatography using 10% ethyl acetate−petroleum ether (v/v) as eluent to furnish the product **14** as a pale yellow amorphous solid (89 mg, 91%); mp 82−84 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.39 (brs, 1H), 8.35 (d, J = 8.4 Hz, 1H), 7.55−7.50 (m, 2H), 7.29−7.24 (m, 1H), 6.80 (brs, 1H), 5.46 (brs, 2H), 3.19 (brs, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.3, 167.9, 155.1 (q, J = 37.5 Hz), 135.2, 131.8, 124.8 (two carbon signals merged probably), 122.8 (two carbon signals merged probably), 115.6 (q, J = 286.9 Hz), 103.0, 87.6, 31.9 ppm. HRMS (ESI$^+$) m/z calculated for $C_{13}H_{12}F_3N_2O_2$ $[M + H]^+$ 285.0851, found 285.0841.

*2-Amino-N-methyl-N-(propa-1,2-dien-1-yl)benzamide (**15**).* To a well-stirred solution of acetylene **S2** (100 mg, 0.53 mmol) in dry DMF was added KOH (179 mg, 3.19 mmol). The reaction was found to be

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completed within 2 min (TLC). It was then quenched with water (5 mL) and extracted with EtOAc (3 × 20 mL). Combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by silica gel (100−200 mesh) column chromatography using 10% EtOAc−petroleum ether (v/v) as eluent to afford **15** as a yellow gum (55 mg, 55%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.22−7.17 (m, 3H), 6.75−6.71 (m, 2H), 5.41−5.39 (m, 2H), 4.43 (brs, 2H), 3.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.7, 169.3, 146.2, 131.2, 128.9, 118.4, 117.2, 116.8, 99.9, 86.9, 32.4 ppm. HRMS (ESI$^+$) *m*/*z* calculated for $C_{11}H_{12}N_2ONa$ $[M + Na]^+$ 211.0847, found 211.0847.

General Procedure for Palladium-Catalyzed Synthesis of 2-(α-Styryl)-2,3-dihydroquinazolin-4-ones 9a,b (Table 2). To a well-stirred solution of $Pd(OAc)_2$ (0.05 equiv) and PPh_3 (0.12 equiv) in dry DMF (4 mL) was sequentially added iodo compound **11** (1 equiv), K_2CO_3 (4 equiv), and allene **13**/**14**/**15** (1 equiv) under an argon atmosphere. The whole reaction mixture was allowed to stir at room temperature for the requisite time (see Table 2) until completion (TLC). DMF was removed *in vacuo*. The resulting mixture was extracted with EtOAc (3 × 20 mL) and washed with water (10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was then purified by (silica gel 100−200 mesh) column chromatography using 10−50% ethyl acetate−petroleum ether (v/v) as eluent to afford the desired products (**9a**, **9b**).

*3-Methyl-2-(1-phenylvinyl)-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9aa**).* Pale brown crystalline solid (68.9 mg, 94% yield); mp 192−193 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86 (dd, *J* = 7.5 Hz, 1.5 Hz, 1H), 7.49 (td, *J* = 7.5 Hz, 1.5 Hz, 2H), 7.42−7.33 (m, 7H), 7.26−7.22 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.45 (s, 1H), 5.31 (d, *J* = 1.5 Hz, 1H), 4.89 (d, *J* = 2.1 Hz, 1H), 2.93 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.5, 144.7, 142.6, 137.4, 135.3, 133.9, 132.6, 129.5, 128.4, 128.2, 127.5, 127.0, 126.9, 125.6, 117.3, 73.8, 33.7, 21.6 ppm (two C signals seemed to overlap with other aromatic carbons); HRMS (EI$^+$) *m*/*z* calculated for $C_{24}H_{22}N_2O_3S$ $[M]^+$ 418.1351, found 418.1352.

*3-Methyl-2-[1-(pyridin-3-yl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9ab**).* Pale yellow solid (53.7 mg, 73% yield); mp 181−182 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.61 (d, *J* = 4.5 Hz, 1H), 8.47 (brs, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.56−7.50 (m, 1H), 7.45−7.35 (m,3H), 7.28−7.24 (m, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.41 (s, 1H), 5.40 (s, 1H), 5.03 (d, *J* = 1.2 Hz, 1H), 2.97 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 149.4, 148.2, 144.9, 139.9, 135.1, 134.1, 133.8, 133.2, 132.9, 129.6, 127.8, 127.7, 126.9, 126.9, 125.4, 123.1, 118.7, 73.6, 33.8, 21.6 ppm; HRMS (FAB$^+$) *m*/*z* calculated for $C_{23}H_{22}N_3O_3S$ $[M + H]^+$ 420.1382, found 420.1377.

*3-Methyl-2-[1-(thiophen-2-yl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9ac**).* White amorphous solid (49.1 mg, 66% yield); mp 182−184 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.62−7.57 (m, 2H), 7.52 (td, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.36 (td, *J* = 7.5 Hz, 1.1 Hz, 1H), 7.26−7.23 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.09−7.06 (m, 1H), 6.39 (s, 1H), 5.47 (s, 1H), 4.73 (s, 1H), 2.89 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 144.9, 139.7, 135.3, 135.1, 133.6, 132.8, 129.5, 127.8, 127.8, 127.5, 127.4, 127.1, 125.9, 125.6, 125.4, 115.6, 73.7, 33.5, 21.7 ppm; HRMS (EI$^+$) *m*/*z* calculated for $C_{22}H_{20}N_2O_3S_2$ $[M]^+$ 424.0915, found 424.0924.

*3-Methyl-2-[1-(p-tolyl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9ad**).* Pale brown amorphous solid (55.3 mg, 73% yield); mp 164−166 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (dd, *J* = 7.5 Hz, 1.5 Hz, 1H), 7.51−7.46 (m, 1H), 7.43−7.40 (m, 1H), 7.34 (td, *J* = 7.4 Hz, 1.3 Hz, 2H), 7.28−7.21 (m, 3H), 7.18−7.11 (m, 4H), 6.43 (s, 1H), 5.28 (d, *J* = 1.2 Hz, 1H), 4.83 (d, *J* = 1.5 Hz, 1H), 2.92 (s, 3H), 2.37−2.35 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.5, 144.7, 142.4, 138.1, 135.4, 134.5, 134.1, 132.7, 129.6, 129.1, 127.6, 127.5, 127.1, 127.0, 126.8, 125.7, 116.6, 73.9, 33.7, 21.7, 21.2 ppm; HRMS (EI$^+$) *m*/*z* calculated for $C_{25}H_{24}N_2O_3S$ $[M]^+$ 432.1508, found 432.1500.

*3-Methyl-1-tosyl-2-{1-[4-(trifluoromethyl)phenyl]vinyl}-2,3-dihydroquinazolin-4(1H)-one (**9ae**).* Yellow amorphous solid (63.0 mg, 74% yield); mp 178−179 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.86 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.50 (td, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.40−7.39 (m, 1H), 7.36 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.45 (t, *J* = 1.5 Hz, 1H), 5.38 (d, *J* = 1.2 Hz, 1H), 4.99 (d, *J* = 1.8 Hz, 1H), 2.95 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 161.4, 144.9, 141.9, 141.0, 135.2, 133.8, 132.8, 130.3 (q, *J* = 32.0 Hz), 129.6, 127.7, 127.7, 127.3, 127.0, 126.9, 125.5, 125.4 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 270.6 Hz), 118.9, 73.7, 33.8, 21.6 ppm; HRMS (EI$^+$) *m*/*z* calculated for $C_{25}H_{21}F_3N_2O_3S$ $[M]^+$ 486.1225, found 486.1216.

*2-[1-(4-Methoxyphenyl)vinyl]-3-methyl-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9af**).* Brown amorphous solid (58.2 mg, 74% yield); mp 150−151 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.52−7.41 (m, 2H), 7.37−7.31 (m, 3H), 7.26−7.22 (m, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.42 (s, 1H), 5.26 (d, *J* = 0.9 Hz, 1H), 4.80 (d, *J* = 1.5 Hz, 1H), 3.84 (s, 3H), 2.92 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 159.4, 144.6, 141.7, 135.3, 133.9, 132.5, 129.6, 129.4, 128.0, 127.4, 126.9, 126.9, 125.6, 115.8, 113.7, 73.8, 55.1, 33.6, 21.5 (one carbon signal has probably merged with other aromatic carbon signals) ppm; HRMS (EI$^+$) *m*/*z* calculated for $C_{25}H_{24}N_2O_4S$ $[M]^+$ 448.1457, found 448.1453.

*Methyl 4-[1-(3-Methyl-4-oxo-1-tosyl-1,2,3,4-tetrahydroquinazolin-2-yl)vinyl]benzoate (**9ag**).* White amorphous solid (71.8 mg, 86% yield); mp 198−200 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, *J* = 8.7 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.54−7.48 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.40−7.35 (m, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.15(d, *J* = 8.1 Hz, 2H), 6.48 (s, 1H), 5.41 (d, *J* = 0.9 Hz, 1H), 4.99 (d, *J* = 1.5 Hz, 1H), 3.96 (s, 3H), 2.97 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7, 161.4, 144.8, 142.2, 141.9, 135.2, 133.9, 132.8, 129.8, 129.7, 129.6, 127.6, 127.6, 127.0, 126.9, 125.5, 118.6, 73.6, 52.1, 33.8, 21.6 ppm (one carbon signal is expected to merge with other aromatic carbon signals); HRMS (EI$^+$) *m*/*z* calculated for $C_{26}H_{24}N_2O_5S$ $[M]^+$ 476.1406, found 476.1397.

*2-[1-(3-Methyl-4-oxo-1-tosyl-1,2,3,4-tetrahydroquinazolin-2-yl)vinyl]benzaldehyde (**9ah**).* Pale yellow amorphous solid (58.7 mg, 75% yield); mp 156−157 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.80 (s, 1H), 7.91−7.87 (m, 2H), 7.58−7.50 (m, 3H), 7.44−7.35 (m, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.38 (s, 1H), 5.11 (d, *J* = 0.9 Hz, 1H), 5.06 (d, *J* = 1.2 Hz, 1H), 3.02 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.6, 161.3, 144.7, 142.5, 139.8, 135.5, 134.2, 133.8, 133.7, 132.8, 130.7, 129.7, 128.6, 127.7, 127.4, 126.8, 126.5, 125.1, 118.8, 73.7, 33.4, 21.6 ppm; HRMS (ESI$^+$) *m*/*z* calculated for $C_{25}H_{23}N_2O_4S$ $[M + H]^+$ 447.1378, found 447.1421.

*3-Methyl-2-[1-(4-nitrophenyl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9ai**).* Pale yellow amorphous solid (53.6 mg, 66% yield); mp 216−217 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.26 (d, *J* = 9 Hz, 2H), 7.90−7.87 (m, 1H), 7.56−7.50 (m, 3H), 7.42−7.37 (m, 2H), 7.28−7.23 (m, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.49 (s, 1H), 5.47 (d, *J* = 1.2 Hz, 1H), 5.09 (d, *J* = 1.5 Hz, 1H), 2.98 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 147.5, 145.1, 143.9, 141.4, 134.9, 133.6, 132.9, 129.6, 127.9, 127.8, 127.7, 126.9, 126.8, 125.3, 123.7, 119.9, 73.5, 33.8, 21.6 ppm; HRMS (ESI$^+$) *m*/*z* calculated for $C_{24}H_{21}N_3O_5SNa$ $[M + Na]^+$ 486.1100, found 486.1096.

*2-[1-(2,4-Dimethoxypyrimidin-5-yl)vinyl]-3-methyl-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9aj**).* White amorphous solid (75.0 mg, 89% yield); mp 182−184 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86 (d, *J* = 7.8 Hz, 1H), 7.61 (s, 1H), 7.54−7.49 (m, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.38−7.33 (m, 1H), 7.26−7.21 (m, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.51 (s, 1H), 5.15 (d, *J* = 1.2 Hz, 1H), 5.01 (d, *J* = 1.8 Hz, 1H), 4.14 (s, 3H), 4.03 (s, 3H), 2.94 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.8, 165.4, 161.3, 157.6, 144.7, 138.2, 135.3, 134.1, 132.8, 129.6, 127.6, 127.5, 126.9, 126.8, 125.4, 119.3, 113.1, 72.9, 54.9, 54.3, 33.8, 21.6 ppm; HRMS (EI$^+$) *m*/*z* calculated for $C_{24}H_{24}N_4O_5S$ $[M]^+$ 480.1467, found 480.1469.

*2-(Buta-1,3-dien-2-yl)-3-methyl-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**9ak**).* Brown amorphous solid (25.2 mg, 39% yield); mp 152−154 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (dd, *J* = 7.5 Hz, 1.5

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Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.53 (td, J = 7.6 Hz, 1.3 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.26−7.23 (m, 2H), 7.14 (d, J = 8.1 Hz, 2H), 6.28 (dd, J = 17.8 Hz, 11.2 Hz, 1H), 6.20 (s, 1H), 5.88 (d, J = 18 Hz, 1H), 5.31 (d, J = 11.4 Hz, 1H), 5.17 (s, 1H), 4.69 (s, 1H), 2.82 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 163.0, 146.4, 140.6, 136.9, 135.4, 135.4, 134.2, 131.1, 129.2, 129.0, 128.9, 128.6, 127.1, 119.4, 118.9, 74.1, 34.9, 23.2 ppm; HRMS (EI$^+$) m/z calculated for $C_{20}H_{20}N_2O_3S$ [M]$^+$ 368.1195, found 368.1185.

*1,3-Dimethyl-5-[1-(3-methyl-4-oxo-1-tosyl-1,2,3,4-tetrahydroquinazolin-2-yl)vinyl]pyrimidine-2,4(1H,3H)-dione (**9al**).* Brown amorphous solid (53.0 mg, 63% yield); mp 160−162 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.92 (d, J = 8.1 Hz, 1H), 7.62−7.54 (m, 2H) 7.42−7.36 (m, 1H), 7.32−7.28 (m, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.99 (s, 1H), 6.58 (s, 1H), 5.28 (s, 1H), 4.93 (d, J = 1.2 Hz, 1H), 3.44−3.43 (m, 6H), 2.88 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.9, 161.0, 151.2, 144.8, 140.8, 136.7, 135.2, 133.8, 132.6, 129.6, 127.6, 127.4, 126.9, 126.5, 124.9, 118.9, 110.9, 71.7, 37.0, 33.2, 27.9, 21.5 ppm; HRMS (ESI$^+$) m/z calculated for $C_{24}H_{24}N_4O_5SNa$ [M + Na]$^+$ 503.1365, found 503.1357.

*3-Methyl-2-(1-phenylvinyl)-2,3-dihydroquinazolin-4(1H)-one (**9ba**).* Yellow gum (41.0 mg, 74% yield from **14**; 50.5 mg, 60% yield from **15**); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93 (d, J = 7.5 Hz, 1H), 7.37 (brs, 5H), 7.28−7.22 (m, 1H), 6.88−6.83(m, 1H), 6.46 (d, J = 7.8 Hz, 1H), 5.59 (s, 1H), 5.43 (s, 1H), 5.24 (s, 1H), 4.30 (brs, 1H), 3.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.6, 144.8, 144.4, 137.9, 133.2, 128.8, 128.3, 127.1, 119.3, 116.2, 114.4, 73.4, 32.8 ppm (two carbon signals probably have merged with other aromatic carbons); HRMS (ESI$^+$) m/z calculated for $C_{17}H_{17}N_2O$ [M + H]$^+$ 265.1341, found 265.1371.

*3-Methyl-2-{1-[4-(trifluoromethyl)phenyl]vinyl}-2,3-dihydroquinazolin-4(1H)-one (**9bb**).* Dark brown amorphous solid (40.7 mg, 58% yield); mp 128−130 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.90 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.28−7.22 (m, 1H), 6.87−6.82 (m, 1H), 6.47 (d, J = 7.8 Hz, 1H), 5.58 (d, J = 1.8 Hz, 1H), 5.48 (s, 1H), 5.34 (d, J = 0.6 Hz, 1H), 4.26 (brs, 1H), 3.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.6, 144.6, 143.9, 141.6, 133.4, 130.2 (q, J = 32.2 Hz), 128.3, 127.7, 125.6 (q, J = 3.7 Hz), 123.9 (q, J = 270.5 Hz), 119.4, 118.1, 116.0, 114.5, 73.6, 32.6 ppm; HRMS (EI$^+$) m/z calculated for $C_{18}H_{15}F_3N_2O$ [M]$^+$ 332.1136, found 332.1144.

*2-[1-(4-Methoxyphenyl)vinyl]-3-methyl-2,3-dihydroquinazolin-4(1H)-one (**9bc**).* Brown amorphous solid (31.1 mg, 50% yield from **14**; 46.0 mg, 49% yield from **15**); mp 113−115 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (d, J = 6.3 Hz, 1H), 7.34−7.31 (m, 2H), 7.22 (dd, J = 7.6 Hz, 1.0 Hz, 1H), 6.90−6.80 (m, 3H), 6.45 (d, J = 8.1 Hz, 1H), 5.56 (s, 1H), 5.38 (s, 1H), 5.16 (s, 1H), 4.27 (brs, 1H), 3.82 (s, 3H), 3.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.6, 159.6, 145.0, 143.7, 133.2, 130.0, 128.3, 128.2, 119.1, 116.0, 115.2, 114.4, 114.1, 73.7, 55.3, 32.5 ppm; HRMS (ESI$^+$) m/z calculated for $C_{18}H_{18}N_2O_2Na$ [M + Na]$^+$ 317.1266, found 317.1258.

*Methyl 4-[1-(3-Methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)vinyl]benzoate (**9bd**).* Brown crystalline solid (56.5 mg, 83% yield from **14**; 82.2 mg, 80% yield from **15**); mp 156−158 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03 (d, J = 8.1 Hz, 2H), 7.92 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.28−7.23 (m, 1H), 6.86 (t, J = 7.5 Hz, 1H), 6.46 (d, J = 7.8 Hz, 1H), 5.61 (s, 1H), 5.51 (s, 1H), 5.33 (s, 1H), 4.28 (brs, 1H), 3.95 (s, 3H), 3.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 163.5, 144.7, 144.1, 142.6, 133.3, 129.9, 129.8, 128.2, 127.2, 119.3, 117.7, 116.1, 114.5, 73.4, 52.2, 32.7 ppm; HRMS (EI$^+$) m/z calculated for $C_{19}H_{18}N_2O_3$ [M]$^+$ 322.1317, found 322.1321.

*2-[1-(2,4-Dimethoxypyrimidin-5-yl)vinyl]-3-methyl-2,3-dihydroquinazolin-4(1H)-one (**9be**).* Brown amorphous solid (57.2 mg, 55% yield); mp 150−152 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (s, 1H), 7.85 (dd, J = 7.6 Hz, 1.3 Hz, 1H), 7.25−7.19 (m, 1H), 6.83−6.78 (m, 1H), 6.47−6.44 (m, 1H), 5.48 (s, 1H), 5.31 (s, 1H), 5.23 (s, 1H), 4.38 (brs, 1H), 4.01 (s, 3H), 3.98 (s, 3H), 3.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.9, 166.2, 164.1, 159.2, 145.3, 140.4, 134.2, 129.1, 120.4, 119.4, 117.5, 115.4, 114.3, 73.2, 55.9, 55.3, 34.1 ppm; HRMS (ESI$^+$) m/z calculated for $C_{17}H_{18}N_4O_3Na$ [M + Na]$^+$ 349.1277, found 349.1257.

General Procedure for One-Pot Bis-heteroannulation (Scheme 2). To a stirred solution of diiodo compound **16a** (38.6 mg, 0.12 mmol) [or **16b** (39.3 mg, 0.12 mmol)] in dry DMF (3 mL) were added K_2CO_3 (129.1 mg, 0.94 mmol) and allenamide **13** (80.0 mg, 0.23 mmol) sequentially. After stirring for a few minutes, $Pd(OAc)_2$ (2.6 mg, 0.01 mmol) and PPh_3 (7.4 mg, 0.03 mmol) were added, and the whole reaction mixture was allowed to stir at rt under an argon atmosphere for the requisite time (see Scheme 2). After completion of the reaction (TLC), DMF was evaporated under reduced pressure and the resulting mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with water (15 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by silica gel (100−200 mesh) column chromatography using 40% ethyl acetate−petroleum ether (v/v) to afford the desired product **17a** (or **17b**).

*2,2′-[1,4-Phenylenebis(ethene-1,1-diyl)]bis[3-methyl-1-tosyl-2,3-dihydroquinazolin-4(1H)-one] (**17a**).* White crystalline solid (44.3 mg, 50% yield); mp 264−265 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86 (d, J = 8.1 Hz, 2H), 7.56−7.51 (m, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.41−7.34 (m, 6H), 7.27−7.25 (m, 4H), 7.15 (d, J = 8.1 Hz, 4H), 6.49 (s, 2H), 5.40 (s, 2H), 4.93 (s, 2H), 2.96 (s, 6H), 2.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.5, 144.7, 142.2, 137.2, 135.3, 133.9, 132.8, 129.5, 127.6, 127.5, 127.2, 126.9, 125.6, 117.3, 73.7, 33.8, 21.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{42}H_{39}N_4O_6S_2$ [M + H]$^+$ 759.2311, found 759.2304.

*2,2′-[Thiophene-2,5-diylbis(ethene-1,1-diyl)]bis[3-methyl-1-tosyl-2,3-dihydroquinazolin-4(1H)-one] (**17b**).* Brown amorphous solid (49.2 mg, 55% yield); mp 236−238 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.89 (d, J = 7.5 Hz, 2H), 7.54−7.49 (m, 8H), 7.39−7.34 (m, 4H), 7.29−7.26 (m, 4H), 6.65 (s, 2H), 4.79 (s, 2H), 4.69 (d, J = 1.2 Hz, 2H), 2.89 (s, 6H), 2.41 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 144.9, 139.6, 135.2, 134.8, 133.6, 132.8, 129.5, 127.8, 127.5, 127.2, 126.7, 125.6, 116.2, 73.5, 33.5, 21.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{40}H_{36}N_4O_6S_3Na$ [M + Na]$^+$ 787.1695, found 787.1693.

Synthesis of Internal Alkyne 18: Reaction of Phenyl Substitute Allenamide 19 with Iodo Compound 11g (Scheme 3). A mixture of iodobenzene (63 mg, 0.31 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.006 mmol), CuI (2 mg, 0.012 mmol), and Et_3N (74 mg, 0.73 mmol) in dry DMF (3.0 mL) was stirred under an argon atmosphere for a few minutes. To a well-stirred solution of this reaction mixture was added terminal alkyne **10** (100 mg, 0.29 mmol) slowly, and stirring was continued for 1 h. After completion of reaction (TLC), the solvent was evaporated under reduced pressure and the resulting residue was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with water (10 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was then purified by silica gel (100−200 mesh) column chromatography using 17% ethyl acetate−petroleum ether (v/v) as eluent to afford the internal alkyne **18**.

*N-Methyl-2-[(4-methylphenyl)sulfonamide]-N-(3-phenylprop-2-yn-1-yl)benzamide (**18**).* Brown amorphous solid (93 mg, 76%); mp = 93−95 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (s, 1H), 7.71−7.62 (m, 3H), 7.47−7.34 (m, 6H), 7.26−7.14 (m, 4H), 4.45 (brs, 1H), 3.65 (brs, 1H), 3.05−2.67 (m, 3H), 2.34 (brs, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.0, 143.5, 136.4, 136.3, 135.9, 131.7, 131.1, 129.4, 128.7, 128.3, 127.1, 125.9, 124.5, 124.3, 83.0, 82.9, 40.1, 36.7, 32.8, 21.3 ppm. HRMS (ESI$^+$) m/z calculated for $C_{24}H_{22}N_2O_3SNa$ [M + Na]$^+$ 441.1249, found 441.1244.

KO^{t}Bu (47 mg, 0.42 mmol) was added to the solution of acetylene **18** (90 mg, 0.21 mmol) in dry DMF (5 mL), and the stirring was continued at rt under an argon atmosphere. The reaction was found to be completed within 15 min (TLC) and quenched with water (3 mL). It was then extracted with EtOAc (3 × 15 mL), and the combined organic extracts were washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Without further purification, the resulting crude compound obtained was used directly for the next palladium-catalyzed cyclization. To a stirred solution of $Pd(OAc)_2$ (2 mg, 0.01 mmol), and PPh_3 (7 mg, 0.02 mmol) in dry DMF were added 4-iodomethylbenzoate **11g** (55 mg, 0.21 mmol), K_2CO_3 (116 mg, 0.84 mmol), and allene **19** (0.21 mmol) sequentially

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at room temperature under an argon atmosphere, and the whole reaction mixture was allowed to stir at room temperature for 5 h. After completion of reaction (TLC), DMF was evaporated under reduced pressure and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by silica gel (100−200 mesh) column chromatography using 17% ethyl acetate−petroleum ether (v/v) as eluent to afford the desired product **20**.

*Methyl (E)-4-[1-(3-Methyl-4-oxo-1-tosyl-1,2,3,4-tetrahydroquinazolin-2-yl)-2-phenylvinyl]benzoate (**20**).* Brown amorphous solid (65.4 mg, 55% yield); mp 180−181 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.02 (dd, J = 6.6 Hz, 1.8 Hz, 2H), 7.89 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.53−7.50 (m, 2H), 7.36−7.34 (m, 1H), 7.23 (dd, J = 6.9 Hz, 1.5 Hz, 2H), 7.14−7.11 (m, 4H), 7.06−7.05 (m, 1H), 7.02−6.99 (m, 2H), 6.73−6.71 (m, 2H), 6.28 (d, J = 1.8 Hz, 1H), 6.27 (brs, 1H), 3.94 (s, 3H), 2.99 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.4, 162.9, 146.3, 143.2, 137.1, 136.0, 135.9, 135.7, 134.4, 132.1, 131.7, 131.2, 131.2, 130.9, 130.7, 129.6, 129.5, 129.3, 129.1, 128.5, 128.4, 126.8, 77.8, 53.7, 35.5, 23.2 ppm; HRMS (FAB$^+$) m/z calculated for $C_{32}H_{29}N_2O_5S$ $[M + H]^+$ 553.1797, found 553.1804.

General Procedure for Synthesis of 3-α-Styryl-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxide 23 (Table 3). *Synthesis of Starting Acetylene Compound **21**.* The acetylene was synthesized in three steps from commercially available *o*-nitrobenzenesulfonyl chloride.

*Synthesis of N-Methyl-2-nitro-N-(prop-2-yn-1-yl)benzenesulfonamide (**S3**).* To a stirred solution of *o*-nitrobenzenesulfonyl chloride (1 g, 4.51 mmol) and Et_3N (548 mg, 5.41 mmol) in dry dichloromethene (10 mL) was added *N*-methylpropargylamine (468 mg, 6.77 mmol) at 0 °C, and the whole reaction mixture was allowed to stir at room temperature for 2 h until completion (TLC). The solvent was evaporated under reduced pressure, and the resulting mixture was extracted with dichloromethane (3 × 20 mL). The combined organic extract was washed with water (15 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel (100−200 mesh) column chromatography using 15% ethyl acetate−petroleum ether (v/v) as eluent to afford the product **S3** as a white solid (848 mg, 74%). The spectral data of the product were in accordance with the reported[26] data. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05−8.02 (m, 1H), 7.73−7.69 (m, 2H), 7.65−7.62 (m, 1H), 4.16 (d, J = 2.4 Hz, 2H), 3.01 (s, 3H), 2.21 (t, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.2, 133.9, 131.6, 131.4, 130.8, 124.0, 76.4, 74.1, 39.6, 34.3 ppm. MS (ESI$^+$) m/z 277.03 $[M + Na]^+$.

*2-Amino-N-methyl-N-(prop-2-yn-1-yl)benzenesulfonamide (**S4**).* Saturated aqueous NH_4Cl (1.15 g, 21.50 mmol) solution was added to the solution of **S3** (840 mg, 3.31 mmol) in MeOH (10 mL). Thereafter, activated Zn (1.075 g, 16.53 mmol) was added to the mixture at room temperature, and the whole reaction mixture was stirred for 2.5 h under an argon atmosphere. After completion of the reaction (TLC), the reaction mixture was then filtered through a sintered funnel and the filtrate was concentrated *in vacuo*. The resulting mixture obtained was diluted with 2N NaOH solution (8 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by silica gel (100−200 mesh) column chromatography using 15% ethyl acetate−petroleum ether (v/v) as eluent to afford pure **S4** as a yellow liquid (422 mg, 57%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.60 (dd, J = 8.1 Hz, 1.5 Hz, 1H), 7.33−7.26 (m, 1H), 6.76 (d, J = 6.9 Hz, 1H), 6.71 (d, J = 8.1 Hz, 1H), 5.05 (brs, 1H), 4.02 (d, J = 2.7 Hz, 2H), 2.87 (s, 3H), 2.16 (t, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.3, 134.3, 130.3, 118.4, 117.7, 117.2, 73.7, 73.7, 39.6, 34.3 ppm. HRMS (ESI$^+$) m/z calculated for $C_{10}H_{12}N_2O_2SNa$ $[M + Na]^+$ 247.0517, found 247.0505.

*N-Methyl-2-[(4-methylphenyl)sulfonamide]-N-(prop-2-yn-1-yl)-benzenesulfonamide (**21**).* To a stirred and cooled (0 °C) solution of **S4** (400 mg, 1.79 mmol) in dry dichloromethane were added pyridine (169 mg, 2.14 mmol) and TsCl (349 mg, 1.84 mmol) sequentially, and the whole reaction mixture was allowed to stir at rt for overnight. The solvent was evaporated under reduced pressure, and the mixture obtained was extracted with dichloromethane. The crude residue obtained was purified by silica gel (100−200 mesh) column chromatography using 15% ethyl acetate−petroleum ether (v/v) as eluent to afford **21** as a white amorphous solid (560 mg, 83%); mp 92−94 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.23 (s, 1H), 7.86 (d, J = 8.4 Hz, 2H), 7.76 (dd, J = 8.1 Hz, 1.5 Hz, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.54−7.48 (m, 1H), 7.35−7.31 (m, 2H), 7.19−7.14 (m, 1H), 4.03 (d, J = 2.1 Hz, 2H), 2.88 (s, 3H), 2.45 (s, 3H), 2.19 (t, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.5, 136.5, 136.2, 134.6, 130.3, 129.9, 127.3, 123.9, 123.3, 119.1, 75.6, 74.6, 39.6, 34.3, 21.6 ppm. HRMS (EI$^+$) m/z calculated for $C_{17}H_{18}N_2O_4S_2$ $[M]^+$ 378.0708, found 378.0711.

Generation of Allenesulphonamide 22 from Acetylene 21 and Subsequent Reactions with Iodo Compounds 11 To Synthesize 3-(α-Styryl)-3,4-dihydro-1,2,4-benzothiadiazine-1,1-dioxides 23. KO^{t}Bu (35.6 mg, 0.32 mmol) was added to the solution of acetylene **21** (60.0 mg, 0.16 mmol) in dry DMF at rt under an argon atmosphere; the reaction was found to be complete within 2 min (TLC). The reaction was quenched with water (5 mL) and extracted with ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product obtained was used directly in the next step without further purification. To a stirred solution of $Pd(OAc)_2$ (1.8 mg, 0.008 mmol) and PPh_3 (5.0 mg, 0.02 mmol) in dry DMF (5 mL) were added iodo compound **11** (0.16 mmol), K_2CO_3 (87.6 mg, 0.64 mmol), and crude allenesulphonamide **22** (0.16 mmol) sequentially, and the whole reaction mixture was heated at 60 °C for the requisite time (see Table 3) under an argon atmosphere. After completion of reaction (TLC), DMF was evaporated under reduced pressure and the resulting residue was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with water (15 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude mixture was purified by silica gel (100−200 mesh) column chromatography using 9−40% ethyl acetate−petroleum ether (v/v) as eluent to afford the pure product **23**.

*2-Methyl-3-(1-phenylvinyl)-4-tosyl-3,4-dihydro-2H-benzo[e]-[1,2,4]thiadiazine-1,1-dioxide (**23a**).* White amorphous solid (48.3 mg, 67% yield); mp 154−155 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77 (dd, J = 8.4 Hz, 0.9 Hz, 1H), 7.60 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 7.50−7.41 (m, 4H), 7.33−7.26 (m, 3H), 7.23−7.18 (m, 2H), 7.10 (d, J = 8.1 Hz, 2H), 6.60 (d, J = 1.2 Hz, 1H), 5.62 (d, J = 0.9 Hz, 1H), 5.58 (d, J = 1.5 Hz, 1H), 2.56 (s, 3H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.9, 143.7, 137.8, 135.5, 134.5, 133.5, 129.9, 129.6, 128.7, 128.6, 128.2, 126.7, 126.0, 125.9, 125.7, 118.9, 77.3, 34.1, 21.7 ppm; HRMS (EI$^+$) m/z calculated for $C_{23}H_{22}N_2O_4S_2$ $[M]^+$ 454.1021, found 454.1016.

*2-Methyl-3-[1-(pyridin-3-yl)vinyl]-4-tosyl-3,4-dihydro-2H-benzo-[e][1,2,4]thiadiazine 1,1-dioxide (**23b**).* White amorphous solid (44.8 mg, 62% yield); mp 162−164 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.71 (d, J = 1.8 Hz, 1H), 8.60−8.59 (m, 1H), 7.83 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 7.8 Hz, 1H), 7.59−7.52 (m, 3H), 7.34−7.26 (m, 2H), 7.22 (d, J = 8.1 Hz, 2H), 6.64 (s, 1H), 5.73−5.72 (m, 2H), 2.71 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.5, 147.8, 145.2, 140.8, 134.9, 134.3, 134.2, 133.6, 133.5, 129.6, 129.2, 128.1, 126.0, 125.9, 125.0, 123.4, 120.4, 76.9, 34.4, 21.7 ppm; HRMS (ESI$^+$) m/z calculated for $C_{22}H_{21}N_3O_4S_2Na$ $[M + Na]^+$ 478.0871, found 478.0866.

*2-Methyl-3-[1-(thiophen-2-yl)vinyl]-4-tosyl-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**23c**).* Yellow amorphous solid (29.2 mg, 40% yield); mp 107−108 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.93 (d, J = 7.8 Hz, 1H), 7.68 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.59−7.56 (m, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.32−7.26 (m, 3H), 7.18 (d, J = 8.4 Hz, 2H), 7.04−7.03 (m, 1H), 6.58 (s, 1H), 5.84 (s, 1H), 5.64 (s, 1H), 2.60 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 144.9, 140.1, 137.2, 135.4, 133.9, 133.6, 129.8, 129.4, 128.2, 127.6, 126.0, 125.9, 125.9, 125.5, 125.1, 116.9, 76.9, 33.4, 21.6 ppm; HRMS (EI$^+$) m/z calculated for $C_{21}H_{20}N_2O_4S_3[M]^+$ 460.0585, found 460.0578.

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*2-Methyl-3-[1-(p-tolyl)vinyl]-4-tosyl-3,4-dihydro-2H-benzo[e]-[1,2,4]thiadiazine-1,1-dioxide (**23d**).* White amorphous solid (46.8 mg, 63% yield); mp 201−202 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.88 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 7.8 Hz, 1.8 Hz, 1H), 7.57−7.53 (m, 3H), 7.42 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 7.5 Hz, 1H), 7.20−7.18 (m, 4H), 6.68 (s, 1H), 5.69 (s, 1H), 5.61 (d, J = 1.2 Hz, 1H), 2.63 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 144.8, 143.3, 138.4, 135.5, 134.7, 134.4, 133.4, 129.6, 129.4, 129.3, 128.1, 126.4, 125.9, 125.8, 125.5, 118.0, 77.1, 33.9, 21.6, 21.2 ppm; HRMS (EI$^+$) m/z calculated for $C_{24}H_{24}N_2O_4S_2$ [M]$^+$ 468.1177, found 468.1172.

*2-Methyl-4-tosyl-3-{1-[4-(trifluoromethyl)phenyl]vinyl}-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**23e**).* White amorphous solid (72.9 mg, 88% yield); mp 71−72 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84 (d, J = 8.1 Hz, 1H), 7.70 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 7.66−7.52 (m, 7H), 7.33−7.26 (m, 1H), 7.21 (d, J = 8.1 Hz, 2H), 6.67 (s, 1H), 5.75−5.73 (m, 2H), 2.68 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.1, 142.6, 141.2, 135.1, 134.2, 133.6, 130.4 (q, J = 32.0 Hz), 129.6, 129.2, 128.0, 127.0, 126.0, 125.9, 125.5 (q, J = 3.7 Hz), 125.1, 120.5, 76.9, 34.3, 21.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{24}H_{21}F_3N_2O_4S_2Na$ [M + Na]$^+$ 545.0792, found 545.0797.

*3-[1-(4-Methoxyphenyl)vinyl]-2-methyl-4-tosyl-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**23f**).* Pale yellow solid (30.0 mg, 39% yield); mp 152−154 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.88 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 8.7 Hz, 2H), 7.30 (d, J = 7.5 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 6.65 (s, 1H), 5.66 (s, 1H), 5.59 (s, 1H), 3.84 (s, 3H), 2.62 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.8, 144.8, 142.8, 135.5, 134.3, 133.4, 133.1, 129.8, 129.4, 128.1, 127.7, 127.6, 125.9, 125.6, 117.3, 113.9, 77.2, 55.3, 33.8, 21.6 ppm; HRMS (EI$^+$) m/z calculated for $C_{24}H_{24}N_2O_5S_2$ [M]$^+$ 484.1127, found 484.1135.

*Methyl 4-[1-(2-Methyl-1,1-dioxido-4-tosyl-3,4-dihydro-2H-benzo-[e][1,2,4]thiadiazin-3-yl)vinyl]benzoate (**23g**).* Brown crystalline solid (42.2 mg, 52% yield); mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.04 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.1 Hz, 1H), 7.68 (dd, J = 7.6 Hz, 1.3 Hz, 1H), 7.57−7.51 (m, 5H), 7.32−7.26 (m, 1H), 7.20 (d, J = 8.1 Hz, 2H), 6.69 (s, 1H), 5.78 (s, 1H), 5.73 (d, J = 1.2 Hz, 1H), 3.94 (s, 3H), 2.66 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7, 145.1, 142.9, 142.1, 135.1, 134.2, 133.6, 130.0, 129.9, 129.6, 129.4, 128.1, 126.7, 126.0, 125.9, 125.2, 120.4, 76.9, 52.2, 34.3, 21,7 ppm; HRMS (ESI$^+$) m/z calculated for $C_{25}H_{24}N_2O_6S_2Na$ [M + Na]$^+$ 535.0973, found 535.0981.

*3-[1-(4-Fluorophenyl)vinyl]-2-methyl-4-tosyl-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**23m**).* White amorphous solid (47.0 mg, 63% yield); mp 172−174 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 7.57−7.46 (m, 5H), 7.32−7.26 (m, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.09−7.04 (m, 2H), 6.61 (s, 1H), 5.66−5.65 (m, 2H), 2.65 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.8 (d, J = 247.5 Hz), 144.9, 142.6, 135.3, 134.3, 133.7 (d, J = 3 Hz), 133.5, 129.5, 128.4 (d, J = 7.5 Hz), 128.1, 125.9 (d, J = 15 Hz), 125.4, 118.9, 115.6, 115.4, 77.2, 33.9, 21.6 ppm (one carbon signal has probably merged with other aromatic carbon signals); HRMS (ESI$^+$) m/z calculated for $C_{23}H_{21}FN_2O_4S_2Na$ [M + Na]$^+$ 495.0825, found 495.0832.

*3-[1-(4-Bromophenyl)vinyl]-2-methyl-4-tosyl-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**23n**).* White amorphous solid (51.5 mg, 61% yield); mp 206−208 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84 (d, J = 8.4 Hz, 1H), 7.68 (dd, J = 7.6 Hz, 1.0 Hz, 1H),7.56−7.49 (m, 4H), 7.37 (d, J = 8.4 Hz, 2H), 7.32−7.26 (m, 2H), 7.19 (d, J = 8.1 Hz, 2H), 6.61 (s, 1H), 5.69−5.66 (m, 2H), 2.65 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.2, 142.9, 136.8, 135.4, 134.5, 133.6, 131.9, 129.8, 129.7, 128.5, 128.3, 126.1, 126.0, 125.5, 122.8, 119.5, 77.4, 34.2, 21.8 ppm; HRMS (ESI$^+$) m/z calculated for $C_{23}H_{21}BrN_2O_4S_2Na$ [M + Na]$^+$ 555.0024, found 555.0026.

Synthesis of 2-(α-Styryl)-quinazolinones 7 and 3-(α-Styryl)-1,2,4-benzothiadiazine-1,1-dioxide 8 (Scheme 4). *Typical Procedure for the Synthesis of 3-Methyl-2-(1-phenylvinyl)-quinazolin-4(3H)-one (**7a**).* To a well-stirred solution of dihydroquinazolinone **9aa** (60.0 mg, 0.14 mmol) in dry DMF (2 mL) was added NaH (60% oil suspension) (28.0 mg, 0.70 mmol), and the whole reaction mixture was allowed to stir at rt under an argon atmosphere for 0.5 h. After complete consumption of the starting material (TLC), the reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by silica gel (100−200 mesh) column chromatography using 13−80% ethyl acetate−petroleum ether (v/v) to afford the pure product **7a**.

*3-Methyl-2-(1-phenylvinyl)quinazolin-4(3H)-one (**7a**).* White amorphous solid (33.1 mg, 88% yield); mp 106−108 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.34−8.33 (m, 1H), 7.81−7.77 (m, 2H), 7.54−7.51 (m, 1H), 7.37−7.35 (m, 5H), 6.05 (s, 1H), 5.71 (s, 1H), 3.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.4, 155.7, 147.4, 144.1, 135.9, 134.3, 129.1, 129.1, 127.6, 127.1, 126.7, 125.8, 120.8, 118.2, 32.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{17}H_{15}N_2O$ [M + H]$^+$ 263.1184, found 263.1159.

*3-Methyl-2-[1-(pyridin-3-yl)vinyl]quinazolin-4(3H)-one (**7b**).* Yellow gum (27.8 mg, 74% yield); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.73 (d, J = 1.8 Hz, 1H), 8.61 (d, J = 4.2 Hz, 1H), 8.34 (d, J = 7.8 Hz, 1H), 7.81−7.77 (m, 2H), 7.66 (d, J = 7.8 Hz, 1H), 7.56−7.53 (m, 1H), 7.32−7.30 (m, 1H), 6.13 (s, 1H), 5.83 (s, 1H), 3.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.2, 154.5, 150.1, 147.3, 147.1, 141.2, 134.5, 133.1, 131.9, 127.6, 127.4, 126.8, 123.7, 120.8, 120.1, 32.7 ppm; HRMS (ESI$^+$) m/z calculated for $C_{16}H_{13}N_3ONa$ [M + Na]$^+$ 286.0956, found 286.0957.

*3-Methyl-2-[1-(thiophen-2-yl)vinyl]quinazolin-4(3H)-one (**7c**).* Brown gum (33.0 mg, 87% yield); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.34 (d, J = 8.4 Hz, 1H), 7.79−7.77 (m, 2H), 7.55−7.52 (m, 1H), 7.30 (d, J = 5.4 Hz, 1H), 6.98−6.96 (m, 1H), 6.82 (d, J = 3.0 Hz, 1H), 5.95 (s, 1H), 5.51 (s, 1H), 3.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.3, 154.6, 147.3, 140.1, 137.9, 134.4, 127.9, 127.7, 127.3, 126.7, 126.5, 126.3, 120.9, 116.2, 32.7 ppm; HRMS (ESI$^+$) m/z calculated for $C_{15}H_{13}N_2OS$ [M + H]$^+$ 269.0749, found 269.0734.

*3-Methyl-2-[1-(p-tolyl)vinyl]quinazolin-4(3H)-one (**7d**).* Pale yellow crystalline solid (29.9 mg, 78% yield); mp 124−126 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.33 (d, J = 7.8 Hz, 1H), 7.80−7.77 (m, 2H), 7.54−7.51 (m, 1H), 7.26−7.24 (m, 2H), 7.16 (d, J = 7.8 Hz, 2H), 5.99 (s, 1H), 5.65 (s, 1H), 3.36 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.4, 155.9, 147.4, 143.9, 139.1, 134.3, 133.1, 129.8, 127.6, 127.1, 126.7, 125.7, 120.8, 117.2, 32.6, 21.2 ppm; HRMS (ESI$^+$) m/z calculated for $C_{18}H_{16}N_2ONa$ [M + Na]$^+$ 299.1160, found 299.1161.

*3-Methyl-2-{1-[4-(trifluoromethyl)phenyl]vinyl}quinazolin-4(3H)-one (**7e**).* Pale yellow amorphous solid (21.0 mg, 52% yield); mp 184−186 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.35 (d, J = 7.8 Hz, 1H), 7.81−7.80 (m, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.58−7.49 (m, 3H), 6.15 (s, 1H), 5.85 (s, 1H), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.2, 154.8, 147.2, 142.9, 139.4, 134.5, 131.0 (q, J = 32.5 Hz), 127.6, 127.4, 126.8, 126.2, 126.2−126.1 (m), 123.8 (q, J = 270.5 Hz), 120.8, 120.5, 32.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{18}H_{14}F_3N_2O$ [M + H]$^+$ 331.1058, found 331.1054.

*2-[1-(4-Methoxyphenyl)vinyl]-3-methylquinazolin-4(3H)-one (**7f**).* Yellow amorphous solid (33.2 mg, 85% yield); mp 156−157 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.33 (d, J = 7.8 Hz, 1H), 7.80−7.78 (m, 2H), 7.54−7.51 (m, 1H), 7.30−7.28 (m, 2H), 6.89−6.87 (m, 2H), 5.93 (s, 1H), 5.58 (s, 1H), 3.81 (s, 3H), 3.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.4, 160.2, 155.9, 147.4, 143.5, 134.3, 128.5, 127.6, 127.2, 127.1, 126.7, 120.8, 116.1, 114.4, 55.3, 32.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{18}H_{16}N_2O_2Na$ [M + Na]$^+$ 315.1109, found 315.1137.

Typical Procedure for the Synthesis of 2-Methyl-3-(1-phenylvinyl)-2*H*-benzo[*e*][1,2,4]thiadiazine-1,1-dioxide (8a). To a well-stirred solution of 1,2,4-benzothiadiazine-1,1-dioxides **23a** (60.0 mg, 0.13 mmol) in dry DMF (5.0 mL) was added NaH (60% oil suspension) (10.4 mg, 0.26 mmol), and the whole reaction mixture was allowed to stir at rt for 1 h under an argon atmosphere. On complete conversion of starting material (TLC), the reaction was quenched with water (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4

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J. Org. Chem. 2016, 81, 6596−6608

and concentrated *in vacuo*. The resulting crude residue was purified by silica gel (100−200 mesh) column chromatography using 10−50% ethyl acetate−petroleum ether (v/v) to afford the pure product **8a**.

*2-Methyl-3-(1-phenylvinyl)-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**8a**).* White amorphous solid, mp 116−118 °C; (22.3 mg, 57% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.91 (dd, J = 7.9 Hz, 1.0 Hz, 1H), 7.74−7.65 (m, 2H), 7.53−7.48 (m, 3H), 7.46−7.39 (m, 3H), 6.02 (s, 1H), 5.93 (s, 1H), 3.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 155.6, 143.9, 142.7, 135.6, 133.5, 129.2, 129.1, 128.2, 127.3, 126.9, 126.4, 121.3, 121.1, 31.7 ppm; HRMS (ESI$^+$) m/z calculated for $C_{16}H_{15}N_2O_2S$ [M + H]$^+$ 299.0854, found 299.0848.

*2-Methyl-3-[1-(pyridin-3-yl)vinyl]-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**8b**).* Yellow gum (19.7 mg, 50% yield); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.85 (d, J = 1.8 Hz, 1H), 8.65 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.92 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.81 (dt, J = 7.8 Hz, 2.1 Hz, 1H), 7.74−7.72 (m, 1H), 7.65 (dd, J = 8.1 Hz, 0.9 Hz, 1H), 7.55−7.52 (m, 1H), 7.38 (dd, J = 8.4 Hz, 4.8 Hz, 1H), 6.11 (s, 1H), 6.07 (s, 1H), 3.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 154.5, 150.1, 147.6, 142.4, 141.0, 133.9, 133.6, 128.3, 127.7, 127.2, 123.8, 123.3, 121.2, 32.2 ppm (one carbon merged with other aromatic carbons); HRMS (ESI$^+$) m/z calculated for $C_{15}H_{14}N_3O_2S$ [M + H]$^+$ 300.0807, found 300.0800.

Synthesis of *Luotonin F* Analogues 28 (Scheme 5). *Synthesis of N-Benzyl-2-[(4-methylphenyl)sulfonamide]-N-(propa-1,2-dien-1-yl)benzamide (**25**).* Precursor acetylene **24** (100.0 mg, 0.24 mmol) synthesized by reported procedure[20a] was treated with KO^{t}Bu (80.5 mg, 0.72 mmol) in dry DMF (4 mL), and the whole reaction mixture was stirred at rt under an argon atmosphere for 2 h. After completion of the reaction (TLC), it was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by silica gel (100−200 mesh) column chromatography using 15% ethyl acetate−petroleum ether (v/v) as eluent.

*N-Benzyl-2-[(4-methylphenyl)sulfonamide]-N-(propa-1,2-dien-1-yl)benzamide (**25**).* Yellow gum (96 mg, 96%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.39 (brs, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.39−7.26 (m, 9H), 7.15−7.11 (m, 1H), 6.89−6.85 (m, 2H), 5.77 (brs, 1H), 5.34−5.32 (m, 2H), 4.69 (brs, 2H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.1, 167.4, 143.8, 136.5, 131.7, 129.5, 129.2, 128.9, 128.5, 127.7, 126.9, 125.8, 125.2, 124.5, 101.8, 87.8, 77.2, 47.9, 21.4 ppm. HRMS (ESI$^+$) m/z calculated for $C_{24}H_{22}N_2O_3SNa$ [M + Na]$^+$ 441.1249, found 441.1235.

*3-Methyl-2-[1-(quinolin-3-yl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**27a**).* Intermediate **27a** was synthesized from **13** (85 mg, 0.25 mmol) adopting the general procedure of the synthesis of product **9** (Table 2) described earlier. The reaction time was 1 h. The crude product was purified by silica gel (100−200 mesh) column chromatography using 30% ethyl acetate−petroleum ether (v/v) as eluent as a brown amorphous solid (100.2 mg, 86% yield); mp 174−176 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.88 (d, J = 2.1 Hz, 1H), 8.41 (brs, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.96−7.88 (m, 2H), 7.78 (t, J = 7.3 Hz, 1H), 7.69−7.63 (m, 1H), 7.52−7.47 (m, 1H), 7.40−7.35 (m, 2H), 7.27−7.25 (m, 2H), 7.15 (d, J = 8.4 Hz, 2H), 6.58 (s, 1H), 5.59 (s, 1H), 5.12 (s, 1H), 2.98 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 148.8, 146.8, 145.0, 139.4, 135.1, 134.4, 133.7, 132.9, 130.3, 130.1, 129.7, 128.7, 128.5, 128.4, 127.8, 127.7, 127.5, 127.4, 127.0, 125.4, 119.3, 73.6, 33.9, 21.6 ppm; HRMS (ESI$^+$) m/z calculated for $C_{27}H_{23}N_3O_3SNa$ [M + Na]$^+$ 492.1358, found 492.1353.

*2-Methyl-3-[1-(quinolin-3-yl)vinyl]-4-tosyl-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-1,1-dioxide (**27b**).* Intermediate **27b** was synthesized from **21** adopting the general procedure of product **23** (Table 3) described earlier. The reaction time was 1.5 h. The crude product was purified by silica gel (100−200 mesh) column chromatography using 35% ethyl acetate−petroleum ether (v/v) as eluent as a white amorphous solid (66.8 mg, 50% yield); mp 184−186 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.02 (d, J = 2.4 Hz, 1H), 8.27 (d, J = 2.1 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.89−7.83 (m, 2H), 7.77−7.70 (m, 2H), 7.62−7.58 (m, 3H), 7.56−7.50 (m, 1H), 7.30 (td, J = 7.7 Hz, 1.0 Hz, 1H), 7.21 (d, J = 8.1 Hz, 2H), 6.77 (d, J = 1.2 Hz, 1H), 5.89 (d, J = 0.9 Hz, 1H), 5.83 (d, J = 1.5 Hz, 1H), 2.73 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.3, 147.9, 145.3, 141.0, 135.3, 134.5, 133.7, 133.3, 130.5, 130.0, 129.8, 129.6, 129.4, 128.5, 128.3, 127.6, 127.3, 126.2, 126.1, 125.3, 120.7, 77.4, 34.5, 21.8 ppm; HRMS (ESI$^+$) m/z calculated for $C_{26}H_{23}N_3O_4S_2Na$ [M + Na]$^+$ 528.1028, found 528.1029.

*3-Benzyl-2-[1-(quinolin-3-yl)vinyl]-1-tosyl-2,3-dihydroquinazolin-4(1H)-one (**27c**).* To a solution of $Pd(OAc)_2$ (2.6 mg, 0.01 mmol) and PPh_3 (7.2 mg, 0.03 mmol) in dry DMF (5 mL) were added 3-iodoquinoline **26**[27] (58.5 mg, 0.23 mmol), K_2CO_3 (126.8 mg, 0.92 mmol), and allene **25** (96 mg, 0.23 mmol) sequentially. The whole reaction mixture was allowed to stir at rt under an argon atmosphere, and the reaction completed after 1 h (TLC). DMF was removed under reduced pressure, and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was then purified by silica gel (100−200 mesh) column chromatography using 25% ethyl acetate−petroleum ether (v/v) as eluent to afford the product **27c** as a white amorphous solid (75.1 mg, 60% yield); mp 103−105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.70 (d, J = 2.1 Hz, 1H), 8.24 (d, J = 1.8 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.96−7.90 (m, 2H), 7.75 (t, J = 7.2 Hz, 1H), 7.60 (t, J = 7.2 Hz, 1H), 7.49−7.43 (m, 7H), 7.37−7.32 (m, 1H), 6.88 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.1 Hz, 2H), 6.72 (s, 1H), 5.45 (s, 1H), 5.06 (s, 1H), 5.01 (d, J = 13.8 Hz, 1H), 4.22 (d, J = 13.8 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 149.2, 147.5, 144.3, 139.6, 135.4, 135.0, 133.6, 133.5, 133.0, 130.2, 130.2, 129.8, 129.4, 129.0, 128.9, 128.5, 128.3, 128.0, 127.3, 127.3, 127.0, 125.9, 125.3, 119.5, 71.3, 49.9, 21.5 ppm; HRMS (ESI$^+$) m/z calculated for $C_{33}H_{28}N_3O_3S$ [M + H]$^+$ 546.1851, found 546.1847.

*3-Methyl-2-[1-(quinolin-3-yl)vinyl]quinazolin-4(3H)-one (**28a**).* To a stirred solution of **27a** (101.4 mg, 0.22 mmol) in dry DMF was added NaH (60% oil suspension) (43.2 mg, 1.08 mmol), and the whole reaction mixture was allowed to stir at rt under an argon atmosphere for 1 h. Upon consumption of the starting material (TLC), the reaction was quenched with water (5 mL) and extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by silica gel (100−200 mesh) column chromatography using 55% ethyl acetate−petroleum ether (v/v) as eluent to afford product **28a** as a yellow amorphous solid (36.0 mg, 53% yield); (overall yield 39% after 3 steps); mp 180−182 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.15 (d, J = 2.1 Hz, 1H), 8.37 (d, J = 8.1 Hz, 1H), 8.13 (d, J = 8.7 Hz, 1H), 7.93 (d, J = 1.8 Hz, 1H), 7.83 (d, J = 3.6 Hz, 2H), 7.77−7.70 (m, 1H), 7.58−7.53 (m, 2H), 7.49−7.46 (m, 1H), 6.29 (s, 1H), 5.91 (s, 1H), 3.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.5, 154.9, 148.0, 147.4, 141.6, 134.7, 132.9, 132.2, 130.5, 129.5, 128.7, 128.6, 128.4, 127.9, 127.7, 127.6, 127.0, 121.1, 120.3, 32.9 ppm; HRMS (ESI$^+$) m/z calculated for $C_{20}H_{15}N_3ONa$ [M + Na]$^+$ 336.1113, found 336.1117.

2-Methyl-3-[1-(quinolin-3-yl)vinyl]-2*H*-benzo[*e*][1,2,4]thiadiazine-1,1-dioxide (28b). Product **28b** was synthesized adopting the procedure of **28a**; the only difference was that 2.0 equiv of NaH (60% oil suspension) was used in this case instead of 5.0 equiv and the reaction time was 1.5 h. Product **28b** was eluted using 40% ethyl acetate−petroleum ether (v/v) as a yellow gum (17.5 mg, 38% yield); (overall yield 19% after 3 steps); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.16 (s, 1H), 8.26−8.14 (m, 2H), 7.85−7.54 (m, 3H), 7.25−7.20 (m, 1H), 6.91−6.82 (m, 3H), 6.26 (s, 1H), 6.13 (s, 1H), 3.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.9, 148.2, 147.9, 142.6, 141.1, 134.1, 133.8, 130.7, 129.8, 129.1, 128.8, 128.5, 127.9, 127.8, 123.2, 121.4, 120.7, 115.5, 32.3 ppm; HRMS (ESI$^+$) m/z calculated for $C_{19}H_{15}N_3O_2SNa$ [M + Na]$^+$ 372.0783, found 372.0785.

*3-Benzyl-2-[1-(quinolin-3-yl)vinyl]quinazolin-4(3H)-one (**28c**).* Product **28c** was prepared adopting the procedure of **28a**, and the reaction time was 2 h. Product **28c** was eluted using 45% ethyl acetate−petroleum ether (v/v) as a yellow gum (33.2 mg, 62% yield); (overall yield 36% after 3 steps); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.06 (d, J = 2.1 Hz, 1H), 8.43−841 (m, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.86−7.80 (m, 3H), 7.74−7.68 (m, 1H), 7.66−7.57 (m, 2H), 7.54−7.49 (m, 1H), 7.14−7.09 (m, 2H), 7.05−7.01 (m, 3H), 6.14 (s, 1H),

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J. Org. Chem. 2016, 81, 6596−6608

5.61 (s, 1H), 5.20 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.5, 154.8, 147.7, 147.3, 140.6, 136.2, 134.9, 133.2, 130.4, 129.7, 129.2, 128.9, 128.6, 128.3, 127.9, 127.8, 127.5, 127.4, 126.7, 121.2, 120.8, 120.3, 115.6, 48.3 ppm; HRMS (ESI$^+$) m/z calculated for $C_{26}H_{20}N_3O$ $[M + H]^+$ 390.1606, found 390.1602.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01242.

Experimental procedures, copies of NMR (^{1}H and ^{13}C), HRMS of representative compounds, 2D NMR data of compound **20**, and tables of crystal data of compounds **9aa**, **9bd**, **23g**, and **7d** (PDF)

X-ray crystallographic data for compounds **7d**, **9aa**, **9bd**, and **23g** (ZIP)

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Notes

The authors declare no competing financial interest.

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(23) Mechanistically, the dihydroquinazolinones **9** and benzothiadiazine-1,1-dioxide variants **23** are formed through intramolecular nucleophilic attack of the nitrogen atom (of amine moiety) to the Π-allylic palladium complex (see ref 19g), which is perhaps generated through carbopalladation of allene by $RPd^{II}I$ resulting from the oxidative addition of aryl/hetoaryl/vinyl iodide (RI) and Pd(0) formed in situ from $Pd(OAc)_2$ and PPh_3.

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J. Org. Chem. 2016, 81, 6596−6608