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Iodine-Catalyzed, Stereo- and Regioselective Synthesis of 4-Arylidine-4*H*-benzo[*d*][1,3]oxazines and their Applications for the Synthesis of Quinazoline 3-Oxides

Wen-Chun Lee,[a] Ho-Chuan Shen,[a] Wan-Ping Hu,[b] Wei-Sheng Lo,[a] Chebrolu Murali,[a] Jaya Kishore Vandavasi,[a] and Jeh-Jeng Wang[a,*]

[a] Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung City 807, Taiwan
E-mail: jjwang@kmu.edu.tw
[b] Department of Biotechnology, Kaohsiung Medical University, Kaohsiung City, Taiwan

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Abstract: 4-Benzylidene-2-aryl-4*H*-benzo[*d*][1,3] oxazines have been synthesized with high stereoselectivity and regioselectivities from 2-alkynylbenzamides in the presence of a catalytic amount of I_2. In the reaction mechanism, iodine plays a key role in two different aspects as a catalyst, such as to activate the alkyne with the iodinium donor which triggers the cascade, and then as a proper acid source to facilitate catalyst recovery. The benzoxazines have been exploited as potential substrates for the synthesis of quinazoline 3-oxide derivatives directly in one step.

Keywords: 6-*exo-dig* cyclization; iodine; quinazoline 3-oxides; regioselectivity; stereoselectivity

Introduction

Benzoxazines and their analogues are a significant class of heterocycles exhibiting various biological properties such as inhibitory activity towards human leukocyte elastase[1] and Clr serine protease enzymes.[2] Numerous benzoxazine analogues were evolved as DNA-binding antitumor agents[3] and also act as progesterone receptor modulators.[4] Several polymeric benzoxazines were explored as heat resistant and electronic materials.[5] As a consequence of this characteristic behaviour of benzoxazine analogues, new methodologies and synthetic routes have been developed in the recent past.[6–8] However, these methodologies require much attention to improve the scope and applicability for the synthesis of a wide range of benzoxazines. Certain cyclization reactions of various alkynyl derivatives by metal- and non-metal-mediated methodologies were developed with different functionally substituted *ortho*-alkynyl substrates having proximity of the reacting functional groups within the molecule that facilitate the intramolecular cyclizations.[9–12] In particular, I_2,[13a] its pertinent reagents[9–11] and metal halide[11] mediated cyclizations were developed to synthesize various oxygen heterocycles. All these methodologies have their own distinct applicability for the construction of various heterocyclic molecules from the corresponding alkynyl precursors.

In recent years, gold and platinum complexes have attracted keen interest of organic chemists by activating the alkyne, where the alkyne activation participates in important molecular transformations, such as cyclization, cycloisomerization, cycloaddition, etc.[9i] Generally, transition metal-mediated cyclizations of 2-alkynylamide **A** may take place *via* two possible modes of cyclizations. *viz.*, 6-*exo*-dig **A1**[14] or 5-*endo*-dig **A2**[14] modes as mentioned in Figure 1. It was found that 1-(*o*-alkynylaryl)ureas are convenient substrates that provide an adequate framework to explore the Au(I)-catalyzed hydroamidation of alkynes to synthesize 6-*exo*-dig compounds.[14b] Synthesis of indoles by the 5-*endo*-dig mode from *o*-iodotrifluoroacetanilide and 1-alkynes in the presence of copper catalyst was also reported by Cacchi et al.[14c] Annula-

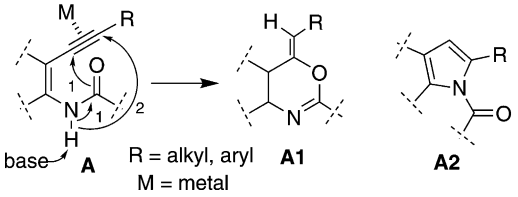


Figure 1. Two possible cyclized intermediates of **A** by metal catalysis.

tion of *o*-alkynylaniline derivatives represents a well-authorized route to indole rings *via* a highly favored 5-*endo*-dig method,[15] whereas in our case we observed specifically the 6-*exo*-dig product without any side product such as indole derivatives. We have obtained exclusively the 6-*exo*-dig derivatives compared to the other reports regarding the annulation. A vast number of reports was aimed to synthesis the indole derivatives with the *N*-substituent on compound **3**.[16–18]

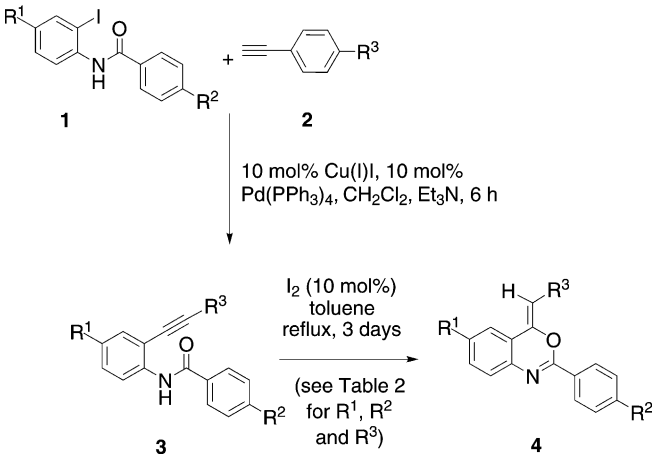
Very recently, Saito et al. reported[14] a regio- and stereoselective synthesis of 4-alkylidene-3,1-benzoxazines *via* the 6-*exo*-dig mode of cyclization of *N*-acyl-alkynylanilines. Although this method emphasized the stereo- and regioselectivities of cyclization, the utilization of equimolar amounts of acid under reflux reaction conditions and transition metal catalysts reveals the dissimilarity in the approach towards the synthesis of various benzoxazines shown in the present communication. We have replaced the palladium with a catalytic amount of iodine for the synthesis of benzoxazines with this new methodology. In addition, the synthesized benzoxazines have been exploited as potential precursors for the synthesis of quinazoline 3-oxides. These quinazoline 3-oxides were reported as excellent precursors for the construction of various heterocycles of biological importance[19] and the synthesis of such derivatives was executed from the corresponding amidoximes by the cyclization method.[19]

Molecular iodine in organic synthesis has been known for a long time. In recent years, molecular iodine has attracted considerable attention as a non-toxic, inexpensive, readily available catalyst for various organic conversions under mild and adaptable conditions to furnish the corresponding products in excellent yields with high selectivity. Mostly, iodine-catalyzed transformations are based on heteroatom rather than carbophilic activation. However, there is no example of benzoxazine synthesis using molecular iodine as a catalyst.[13]

Results and Discussion

Herein, we report an expedient I_2-catalyzed cyclization approach for the synthesis of benzoxazines **4** and their applications for the synthesis of the quinazoline 3-oxides directly in one step. When alkynylamide **3** (prepared from **1** and **2**) reacted with 10 mol% iodine in toluene solvent at reflux temperature, it underwent a cyclization to furnish an unexpected product, the benzoxazine **4** (Scheme 1).

We applied this methodology for the synthesis of differentially substituted 4-benzylidene-4*H*-benzo[*d*]-[1,3]oxazines from various substituted 2-alkylidene-benzamides. In the present context, the 6-*exo*-dig mode of cyclization is observed as predominant path-



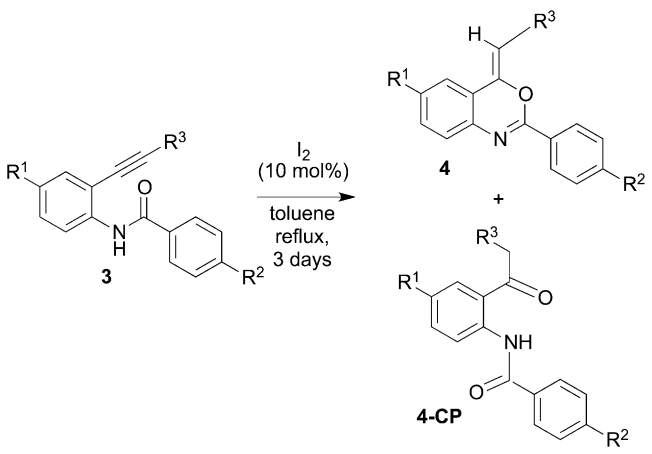
Scheme 1. Cyclization of **3** in the presence of I_2 to obtain benzoxazines **4**.

way (**A1**, Figure 1) during the construction of the benzoxazines. The present observation is significant because of the high regio- and stereoselectivity of the benzoxazine product formation during this electrophilic cyclization reaction. Initial optimization of the reaction was performed in different solvents, from which the toluene is found to be of best solvent system (Table 1, entry 7). The reaction was further optimized with different quantities of I_2 with **3a** and the results are summarized in Table 1. The initial reaction with 1.0 equiv. of I_2 resulted in an 89% yield of the desired product.

Furthermore, the reaction was carried out by varying the amount of I_2. Among the four different reaction conditions used with **3a** (entries 7, 10–12), a good yield of the cyclized product is obtained in the presence of 10 mol% of I_2 in toluene at reflux temperature for 3 days (entry 7).

With these preliminary optimized reaction conditions in hand we further explored the scope and limitations of the cyclization with different examples of the various alkynyl amides and the results are summarized in Table 2. Substrates bearing different functional group combinations as the R^1, R^2 and R^3 positions in **3** have been screened to evaluate the synthetic feasibility for the product formation (entries 1–20). Good to excellent yields were obtained in majority of the cases except for compounds **4e** and **4f**. The presence of the aromatic alkyne is desirable to promote the cyclization which was verified further by choosing some substrates having trimethylsilylacetylene, terminal acetylenes and alkyl groups at the R^3 position (entries 16–18): with the butyl group at the R^3 position the reaction did not suceed and led to the formation of compound **4-CP** (entry 18). When the phenyl substituent was replaced with an aliphatic group such as vinylbenzene or ethyl chain at the amide position the desired product was obtained in a minor quantity and

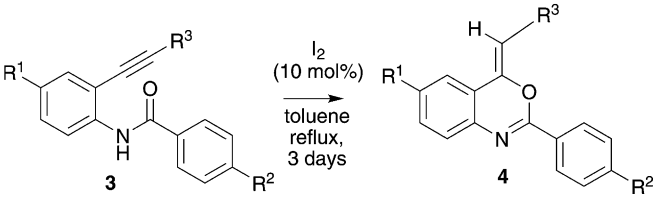
Table 1. Optimization of the reaction conditions for the cyclization of compound **3** to **4**.[a]



Entry	Solvent	I_2 (equiv.)	**4** [%]	**4-CP** [%]
1	MeCN	10 mol%	0	100
2	THF	10 mol%	trace	0
3	DMF	10 mol%	18	72
4	CH_2Cl_2	10 mol%	65	24
5[b]	MeOH	10 mol%	0	15
6	DMSO	10 mol%	22	75
7	toluene	10 mol%	95	0
8[c]	CH_2Cl_2	1.0 equiv.	60	14
9[d]	CH_2Cl_2	30 mol%	61	20
10[c]	toluene	1.0 equiv.	89	0
11[d]	toluene	30 mol%	90	0
12	toluene	5.0 equiv.	92	0

[a] Reflux for 3 days.
[b] Unreacted **3**.
[c] Reaction time 1 day.
[d] Reaction time 2 days.

Table 2. Cyclization of various alkynylamides **3** in the presence of I_2 as catalyst[a]



Entry	**3**	R^1	R^2	R^3	**4**	Yield [%]
1	**3a**	H	H	Ph	**4a**	95
2	**3b**	H	F	Ph	**4b**	71
3	**3c**	H	Cl	Ph	**4c**	73
4	**3d**	H	NO_2	Ph	**4d**	77
5	**3e**	H	CF_3	Ph	**4e**	54[c]
6	**3f**	H	CH_3	Ph	**4f**	46[c]
7	**3g**	CF_3	H	Ph	**4g**	76
8	**3h**	CF_3	F	Ph	**4h**	88
9	**3i**	CF_3	Cl	Ph	**4i**	73
10	**3j**	CF_3	Cl	*p*-FC_6H_4	**4j**	71
11	**3k**	H	NO_2	*p*-FC_6H_4	**4k**	76[b]
12	**3l**	H	Cl	*p*-FC_6H_4	**4l**	70
13	**3m**	H	CF_3	*p*-FC_6H_4	**4m**	65[b]
14	**3n**	H	H	*p*-FC_6H_4	**4n**	92
15	**3o**	H	NO_2	*P*-EtC_6H_4	**4o**	65
16	**3p**	H	NO_2	TMS	**4p**[d]	
17	**3q**	H	H	H	**4q**[e]	
18	**3r**	H	H	butyl	**4r**[f]	
19	**3s**	H	–[g]	Ph	**4s**	20
20	**3t**	H	–[h]	Ph	**4t**	20

[a] *Reaction conditions:* Compound **3** (1.0 mmol), I_2 (10 mol%), dry toluene (10.0 mL), reflux for 3 days.
[b] 1.0 equiv. of I_2 was used.
[c] Reaction time: 5 days.
[d] Complex mixture of products.
[e] No reaction.
[f] Compound **4-CP** was observed.
[g] Phenyl substituent replaced with vinylbenzene.
[h] Phenyl substituent replaced with an ethyl chain.

the major product was compound **4-CP**. (entries 19 and 20). The stereochemistry of the cyclized product was confirmed by the NOESY analysis of the majority of the compounds **4** (see Supporting Information for details). Structure of the product **4a** is evidenced by a single crystal X-ray analysis (Figure 2).

The plausible mechanism for the formation of the benzoxazines **4a** is depicted in Scheme 2. The initially formed iodo complex **5** undergoes the electrophilic cyclization leading to the formation of intermediate **6** which, in turn, reacts with *in situ* generated HI to furnish the benzoxazine **4a** with retention of the Z-stereochemistry along with the regeneration of I_2. We also carried out the reaction of compound **3a** with 10 mol% HI but the reaction did not progress to the formation of **4a**. In order to check the possible formation of the intermediate **6** and HI during the reaction, compound **3a** was reacted with 10 mol% I_2 along with the addition of $NaHCO_3$ (3.0 equiv.) in toluene at room temperature; this furnished the iodobenzoxazine **6** as a sole product. Presumably, the formed HI could be quenched by the base to pause the reaction at the iodide intermediate stage. Furthermore, the isolated compound **6** was treated with 1.0 equiv. HI at 0 °C for 3 h to obtain **4a** (70% yield).

These control experiments evidently support the formation of HI during the reaction but its presence alone cannot play a role in the direct conversion of **3a** to **4a**. The compound **3a** was found to be unchanged after heating in toluene without I_2 under reflux conditions. This experiment was performed to rule out the possibility of lingering traces of the metal[20] along with the substrates that were prepared by using transition metal catalysts.

In the proposed mechanism, which is was well supported by the experimental details, iodine participates in two different roles as a catalyst, first the iodonium

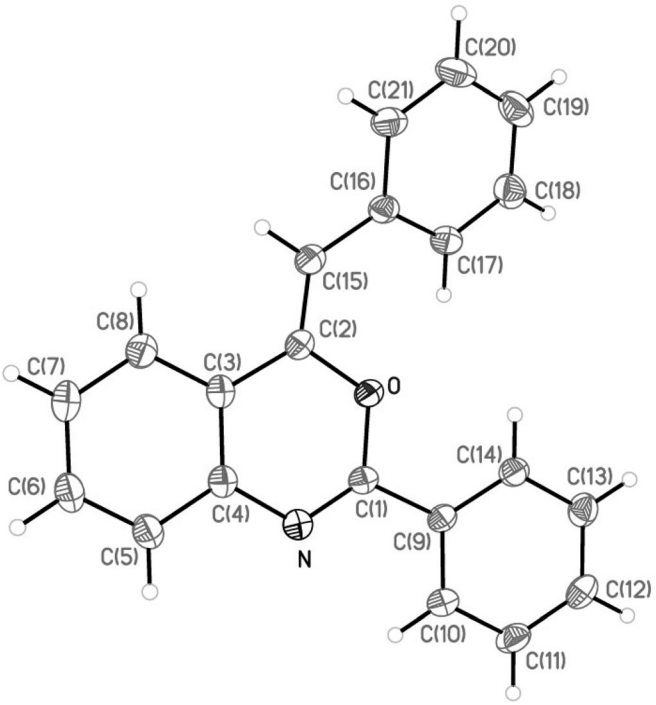
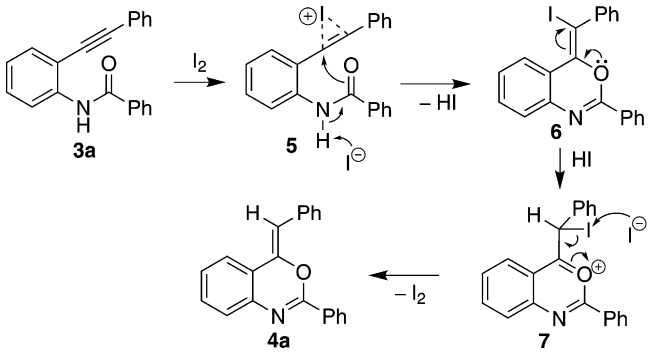


Figure 2. ORTEP plot of **4a**.

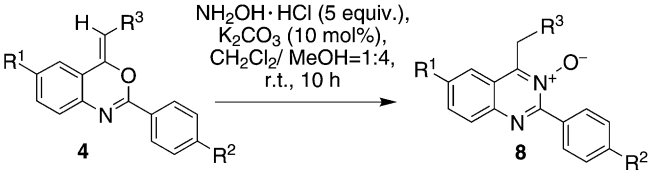


Scheme 2. Plausible mechanism for the formation of benzoxazine **4a**.

donor activates the alkyne which triggers the cascade and then as a proper acid source to facilitate catalyst recovery. Thus, the I_2-catalyzed cyclization of **3** showed the synthetic feasibility for the formation of benzoxazines **4** and provided good yields in the range of 46–95%.

All benzoxazines with various substitutions have been converted to the quinazoline 3-oxides **8** with moderate to good yields (Table 3). A plaussible mechanism for this one-pot approach for the synthesis of *N*-oxides **8** is depicted in the Scheme 3. Initial attack of NH_2OH on the sp^2 carbon (C-1) of the oxazine followed by the H^+ transfer could result in ring opening to form intermediate **10**. Subsequent cyclization of the *N*-hydroxyimidamide followed by elimination of

Table 3. Synthesis of quinazoline 3-oxides **8** from benzoxazines **5**.[a]



Entry	**4**	R^1	R^2	R^3	**8**	Yield [%]
1	**4a**	H	H	Ph	**8a**	75
2	**4b**	H	F	Ph	**8b**	77
3	**4c**	H	Cl	Ph	**8c**	68
4	**4d**	H	NO_2	Ph	**8d**	79
5	**4e**	H	CF_3	Ph	**8e**	86
6	**4f**	H	Me	Ph	**8f**	66
7	**4g**	CF_3	H	Ph	**8g**	83
8	**4h**	CF_3	F	Ph	**8h**	81
9	**4i**	CF_3	Cl	Ph	**8i**	36[b]
10	**4j**	CF_3	Cl	*p*-FC_6H_4	**8j**	31
11	**4k**	H	NO_2	*p*-FC_6H_4	**8k**	69
12	**4l**	H	Cl	*p*-FC_6H_4	**8l**	81
13	**4m**	H	CF_3	*p*-FC_6H_4	**8m**	91
14	**4n**	H	H	*p*-FC_6H_4	**8n**	54
15	**4o**	H	NO_2	*p*-EtC_6H_4	**8o**	83

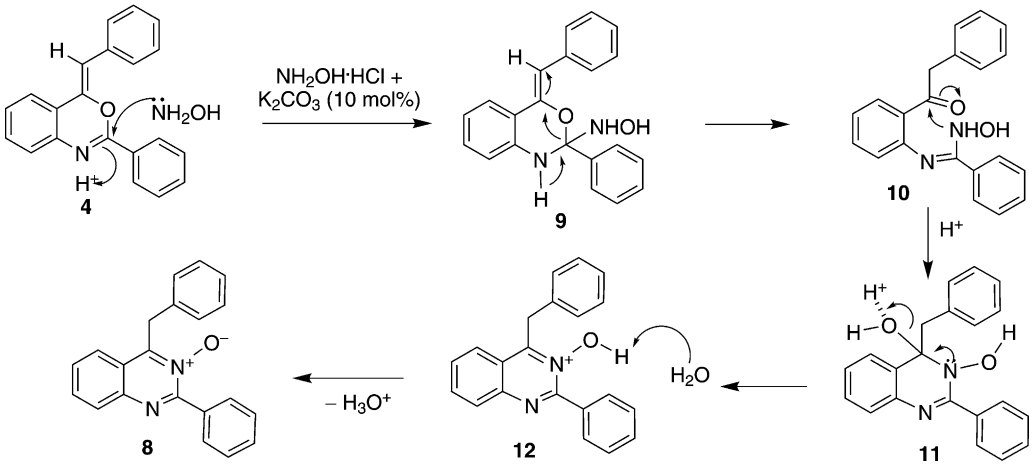
[a] *Reaction conditions:* compound **4** (1.0 mmol), NH_2OH·HCl (1.0 mmol), methanol and dichloromethane (10 mL, 4:1), and K_2CO_3 (1 mol%), room temperature for 10 h.

[b] Mixture of products formed.

H_2O will generate the *N*-oxide. Biological studies of the two *N*-oxides (**8d** and **8k**) have shown the promising results. These two compounds were found to be suitable for photodynamic therapy (PDT) applications against melanoma as well as oral cancer cell lines[21] (see see the Supporting Information for details).

Conclusions

In conclusion, we have developed a highly regio- and stereoselective synthesis of benzoxazines with catalytic I_2. This novel method was able to replace the palladium with iodine to synthesize the benzoxazines. For a long time there was a competition between the 5-*endo*-dig and 6-*exo*-dig product formation and, even though the previous reports furnish the 5-*endo*-dig product with the 6-*exo*-dig product as a side product, in our case we have been obtained the 6-*exo*-dig product exclusively. To the best of our knowledge, the synthesis of benzoxazines in the presence of molecular iodine as a catalyst is a novel pathway and this is the first example of its use for the synthesis of benzoxazines. The proposed mechanism, which is well endorsed by the experimental details, shows that iodine has two different roles as catalyst, (i) alkyne activa-



Scheme 3. Plausible mechanism for the formation of quinazoline 3-oxides **8**.

tion by the iodonium donor that triggers the cascade and then (ii) a proper acid source to facilitate the catalyst recovery. Mostly, iodine-catalyzed transformations are based on heteroatom rather than carbophilic activation.

It is noteworthy to mention that the benzoxazines thus synthesized have been exploited as potential precursors for the efficient and one-pot synthesis of quinazoline 3-oxides. Some compounds were found to be suitable for photodynamic therapy (PDT) applications against melanoma as well as oral cancer cell lines. Further biological studies of the synthesized benzoxazine molecules are in progress.

Experimental Section

General Procedure for the Synthesis of *N*-(2-Iodoaryl)amides 1a–1p

Compounds **1a**–**1p** were prepared and characterized according to the modified literature procedure[1] as follows.

To an ice-cooled solution of the corresponding 2-iodoaniline (1.0 mmol) and triethylamine (10 mL) in dry toluene (10 mL) was added the corresponding benzoyl chloride (1.5 mmol) and the reaction mixture was stirred under an argon atmosphere for 6 h and reaction was monitored by TLC analysis. The crude product was extracted with ethyl acetate followed by washing with water and saturated $NaHCO_3$ solution and drying over anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure and the crude compound obtained was purified by column chromatography using ethyl acetate and hexane solvent system to furnish amides **1a**–**1p**.

General Procedure for Synthesis of 2-Alkynylarylamides 3a–3p

A mixture of the corresponding iodo compound **1** (1.0 mmol), the corresponding terminal alkyne (1.5 mmol), $Pd(PPh_3)_4$ (10 mol%) and CuI (10 mol%) was taken up in dry THF (5 mL) and charged with triethylamine (*ca.* 10 mL) in a flask under an argon atmosphere. The reaction mixture was stirred for 4 h and the reaction was monitered by TLC analysis. The formed product was extracted with ethyl acetate by washing with water, brine and followed by drying over anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure and the crude residue was chromatographed over silica gel to obtain product.

***N*-[2-(Phenylethynyl)phenyl]benzamide (3a):** The title compound was prepared according to the general procedure and purified by column chromatography to furnish a white solid; yield: 90%; mp 103–105 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.96$ (bs, 1H), 8.63 (d, $J = 8.4$ Hz, 1H), 7.96 (d, $J = 8.0$ Hz, 2H), 7.59–7.38 (m, 10H), 7.12 (td, $J = 8.0$ and 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 165.1$, 138.1, 134.9, 132.0, 131.5, 131.4, 129.9, 129.0, 128.9, 128.6, 126.9, 123.5, 122.2, 119.1, 112.2, 96.9, 84.4; HR-MS (ESI): $m/z =$ 320.1048, calcd. for $C_{21}H_{15}NONa$: 320.1051; anal. calcd. for $C_{21}H_{15}NO$: C 84.82, H 5.08, N 4.71; found: C 84.75, H 5.10, N 4.70.

4-Fluoro-*N*-[2-(phenylethynyl)phenyl]benzamide (3b): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 75%; mp 134–136 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.86$ (bs, 1H), 8.58 (d, $J = 8.4$ Hz, 1H), 7.98–7.93 (m. 2H), 7.55–7.50 (m, 3H), 7.43–7.38 (m, 4H), 7.18–7.10 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 166.3$, 163.8 (d, $J = 29.9$ Hz), 138.8, 131.5, 131.3, 131.1, 131.0 (d, $J =$ 6.2 Hz), 129.3 (d, $J = 9.1$ Hz), 129.1, 128.7, 123.6, 122.1, 119.1, 115.9 (d, $J = 22.0$ Hz), 112.2, 97.0, 84.4; HR-MS (ESI): $m/z = 338.0958$, calcd. for $C_{21}H_{14}FNONa$: 338.0957; anal. calcd. for $C_{21}H_{14}FNO$: C 79.98, H 4.47, N 4.44; found: C 79.72, H 4.52, N 4.40.

4-Chloro-*N*-[2-(phenylethynyl)phenyl]benzamide (3c): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 70%; mp 135–137 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.86$ (bs, 1H), 8.56 (d, $J = 8.0$ Hz, 1H), 7.86 (d, $J = 8.8$ Hz, 2H), 7.53–7.37 (m, 9H), 7.11 (td, $J = 8.0$ and 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 163.8$, 138.7, 138.3, 133.1, 131.4, 131.2, 129.8, 129.1, 129.0, 128.6, 128.3, 123.7, 122.0, 119.1, 112.2, 97.0, 84.3; HR-MS (ESI): $m/z =$

354.0663, calcd. for $C_{21}H_{14}ClNO$ $(M+H)^+$: 354.0662; anal. calcd. for $C_{21}H_{13}ClNO$: C 76.02, H 4.25, N 4.22; found: C 75.78, H 4.34, N 4.20.

4-Nitro-*N*-[2-(phenylethynyl)phenyl]benzamide (3d): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 87%; mp 160–162 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.92$ (bs, 1H), 8.58 (d, $J = 8.4$ Hz, 1H), 8.32 (d, $J = 8.0$ Hz, 2H), 8.11 (d, $J = 8.0$ Hz, 2H), 7.57–7.40 (m, 7H), 7.17 (t, $J = 8.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 162.8$, 149.8, 140.3, 138.2, 131.7, 131.3, 129.9, 129.3, 128.8, 128.1, 124.3, 124.1, 121.8, 119.3, 112.6, 97.3, 84.1; HR-MS (ESI): $m/z = 365.0906$, calcd. for $C_{21}H_{14}N_2O_3Na$: 365.0902; anal. calcd. for $C_{21}H_{14}N_2O_3$: C 73.68, H 4.12, N 8.18; found: C 73.15, H 4.16, N 8.12.

***N*-[2-(Phenylethynyl)phenyl]-4-(trifluoromethyl)benzamide (3e):** The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 88%; mp 153–155 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.92$ (bs, 1H), 8.58 (d, $J = 8.0$ Hz, 1H), 8.05 (d, $J = 8.0$ Hz, 2H), 7.73 (d, $J = 8.0$ Hz, 2H), 7.56–7.38 (m, 7H), 7.14 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 163.6$, 138.5, 138.1, 133.7 (q, $J = 33.0$ Hz), 131.6, 131.3, 129.9, 129.2, 128.7, 127.4, 125.9 (q, $J = 3.8$ Hz), 124.0, 123.5 (q, $J = 270.0$ Hz), 122.0, 119.3, 112.5, 97.2, 84.2; HR-MS (ESI): $m/z = 366.1104$, calcd. for $C_{22}H_{15}F_3NONa$: 366.1106; anal. calcd. for $C_{22}H_{15}F_3NO$: C 72.32, H 3.86, N 3.83; found: C 72.36, H 3.85, N 3.86.

4-Methyl-*N*-[2-(phenylethynyl)phenyl]benzamide (3f): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 78%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.93$ (brs, 1H), 8.62 (d, $J = 8.4$ Hz, 1H), 7.87 (d, $J = 1.6$ Hz, 2H), 7.57–7.52 (m, 3H), 7.43–7.38 (m, 4H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.10 (dt, $J = 8.0$ Hz, $J = 1.21$ Hz, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 165.2$, 142.6, 139.2, 132.0, 131.5, 131.4, 129.9, 129.5, 128.9, 128.6, 127.0, 123.4, 122.3, 119.1, 112.1, 96.9, 84.5, 21.5; HR-MS (ESI): $m/z = 312.1390$, calcd. for $C_{22}H_{17}NO$ $[(M+H)^+]$: 312.1383; anal. calcd for $C_{22}H_{17}NO$: C 84.86, H 5.50, N 4.50; found: C 84.65, H 5.55, N 4.48.

***N*-[2-(Phenylethynyl)-4-(trifluoromethyl)phenyl]benzamide (3g):** The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 81%; mp 127–129 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 9.04$ (bs, 1H), 8.76 (d, $J = 8.8$ Hz, 1H), 7.95 (d, $J = 8.0$ Hz, 2H), 7.78 (s, 1H), 7.63–7.37 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 165.1$, 141.6, 134.2, 132.4, 131.4, 129.4, 128.9, 128.7, 128.6, 128.5, 127.0, 126.6 (q, $J = 3.8$ Hz), 125.5 (q, $J = 32.0$ Hz), 123.0 (q, $J = 270.0$ Hz), 121.5, 118.8, 112.4, 98.2, 83.0; HR-MS (ESI): $m/z = 338.0922$, calcd. for $C_{22}H_{14}F_3NONa$: 338.0925; anal. calcd. for $C_{22}H_{14}F_3NO$: C 72.32, H 3.86, N 3.83; found: C 72.59, H 4.04, N 3.75.

4-Fluoro-*N*-[2-(phenylethynyl)-4-(trifluoromethyl)phenyl]benzamide (3h): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 72%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.97$ (brs, 1H), 8.74 (d, $J = 8.8$ Hz, 1H), 7.99–7.93 (m, 2H), 7.80 (d, $J = 2.0$ Hz, 1H), 7.64 (dd, $J = 8.8$ Hz, 2.0 Hz, 1H), 7.57–7.53 (m, 2H), 7.48–7.39 (m, 3H), 7.18 (t, $J = 8.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 166.5$, 164.1 (d, $J = 10.6$ Hz), 141.5, 131.5, 130.5 (d, $J = 3.1$ Hz), 129.6, 129.5 (d, $J = 8.2$ Hz), 128.8, 128.6 (q, $J = 3.8$ Hz), 127.7, 126.7 (q, $J = 3.8$ Hz), 125.7 (q, $J = 33.4$ Hz), 125.0, 123.3 (q, $J = 270.3$ Hz), 122.3, 121.5, 118.9, 116.1 (d, $J = 22$ Hz); HR-MS (ESI): $m/z = 384.1013$, calcd. for $C_{22}H_{14}FNO$: 384.1013; anal. calcd. for $C_{22}H_{13}F_4NO$: C 68.93, H 3.42, N 3.65; found: C 68.87, H 3.42, N 3.68.

4-Chloro-*N*-[2-(phenylethynyl)-4-(trifluoromethyl)phenyl]benzamide (3i): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 66%; mp 178–180 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.97$(s, 1H), 8.74 (d, $J = 8.8$ Hz, 1H), 7.88 (d, $J = 8.8$ Hz, 2H), 7.80 (s, 1H), 7.64 (d, $J = 8.8$ Hz, 1H), 7.56–7.53 (m, 2H), 7.48 (s, 1H), 7.46–7.40 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 164.0$, 141.4, 138.9, 132.6, 131.5, 129.6, 129.3, 128.8, 128.6 (q, $J = 3.8$ Hz), 126.7 (q, $J = 3.8$ Hz), 125.7 (q, $J = 33.0$ Hz), 123.5 (q, $J = 270.0$ Hz), 121.4, 118.9, 112.6, 98.3, 82.9; HR-MS (ESI): $m/z = 422.0537$, calcd. for $C_{22}H_{13}ClF_3NONa$: 422.0535; anal. calcd. for $C_{22}H_{13}ClF_3NO$: C 66.09, H 3.28, N 3.50; found: C 66.08, H 3.28, N 3.49.

4-Chloro-*N*-[2-(4-fluorophenylethynyl)-4-trifluoromethylphenyl]benzamide (3j): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 74%. ^{1}H NMR (DMSO-d_6, 400 MHz): $\delta = 10.35$ (brs, 1H), 8.07–7.97 (m, 4H), 7.81 (d, $J = 8.0$ Hz), 7.71–7.55 (m, 4H), 7.29 (t, $J = 8.0$ Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): $\delta = 164.5$, 142.3, 137.1, 133.9, 133.8 (d, $J = 8.3$ Hz), 132.6, 129.7, 128.8 (d, $J = 18.2$ Hz), 126.0, 125.3, 123.4 (q, $J = 268.5$ Hz), 117.9 (d, $J = 2.9$ Hz), 116.3, 116.1, 95.07, 84.6; HR-MS (ESI): $m/z = 416.0484$, calcd. for $C_{22}H_{12}ClF_4NO$: 416.0478.

***N*-{2-[(4-Fluorophenyl)ethynyl]phenyl}-4-nitrobenzamide (3k):** The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 83%; mp 176–178 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.84$ (bs, 1H), 8.54 (d, $J = 8.4$ Hz, 1H), 8.32 (d, $J = 8.8$ Hz, 2H), 8.08 (d, $J = 8.8$ Hz, 2H), 7.67–7.41 (m, 4H), 7.16 (td, $J = 7.6$ Hz and 1.2 Hz, 1H), 7.11 (t, $J = 8.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 164.2$, 162.8, 161.7, 149.8, 140.2, 138.2, 133.3 (d, $J = 8.4$ Hz), 131.7, 130.0, 128.1, 124.3, 124.1, 119.4, 118.0, 117.9, 116.2 (d, $J = 22.1$ Hz), 112.4, 96.1, 83.8; HR-MS (ESI): $m/z = 361.0987$, calcd. for $C_{21}H_{14}FN_2O_3$: 361.0988; anal. calcd. for $C_{21}H_{13}FN_2O_3$: C 70.0, H 3.64, N 7.77; found: C 69.99, H 3.55, N 7.73.

4-Chloro-*N*-{2-[(4fluorophenyl)ethynyl]phenyl}benzamide (3l): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 82%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 8.8$ (brs, 1H), 8.56 (d, $J = 8.0$ Hz, 1H), 7.86 (d, $J = 8.4$ Hz, 2H), 7.59–7.36 (m, 6H), 7.19–7.02 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 164.0$ (d, $J = 24.0$ Hz), 161.7, 138.6 (d, $J = 34.1$ Hz), 133.3 (d, $J = 9.1$ Hz), 131.6, 130.0, 129.2, 128.3, 123.8, 119.3, 118.2, 116.1 (d, $J = 22.0$ Hz), 112.2, 95.9, 84.1; HR-MS (ESI): $m/z = 348.0605$, calcd. for $C_{21}H_{13}ClFNO$: 349.0670; anal. calcd. for $C_{21}H_{13}ClFNO$: C 72.11, H 3.75, N 4.00; found: C 71.82, H 3.76, N 3.99.

***N*-{2-[(4-Fluorophenyl)ethynyl]phenyl}-4-(trifluoromethyl)benzamide (3m):** The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 78%; mp

132–134 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.85 (s, 1H), 8.58 (d, J = 8.4 Hz, 1H), 8.11–8.03 (m, 2H), 7.86–7.72 (m, 3H), 7.59–7.38 (m, 4H), 7.19–7.07 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 163.9 (d, J = 58.4 Hz), 163.6, 161.7, 138.9, 138.5, 138.1 (q, J = 40.1 Hz), 133.3 (d, J = 8.3 Hz), 131.7, 130.2, 130.0, 129.5, 127.6, 127.4, 125.98, 125.95, 125.91, 123.0 (q, J = 277.4 Hz), 118.1, 116.1 (d, J = 22.8 Hz), 112.4, 96.0, 83.9 (d, J = 1.9 Hz); HR-MS (ESI): m/z = 382.0859, calcd. for $C_{22}H_{13}ClFNO$: 383.0933; anal. calcd. for $C_{22}H_{13}F_4NO$: C 68.93, H 3.42, N 3.65; found: C 67.18, H 3.39, N 3.72.

4-Fluoro-*N*-[2-(phenylethynyl)phenyl]benzamide (3n): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 75%; mp 134–136 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.86 (bs, 1H), 8.58 (d, J = 8.4 Hz, 1H), 7.98–7.93 (m, 2H), 7.55–7.50 (m, 3H), 7.43–7.38 (m, 4H), 7.18–7.10 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 166.3, 163.8 (d, J = 21.2 Hz), 138.8, 131.5, 131.3, 131.1 (d, J = 3.0 Hz), 129.9, 129.4 (d, J = 9.1 Hz), 129.1, 128.7, 123.6, 122.1, 119.1, 115.9 (d, J = 22.0 Hz), 112.2, 97.0, 84.4; HR-MS (ESI): m/z = 316.1132, calcd. for $C_{21}H_{14}FNO$: 316.1135; anal. calcd. for $C_{21}H_{14}FNO$: C 79.98, H 4.47, N 4.44; found: C 79.85, H 4.50, N 4.40.

***N*-{2-[(4-Ethylphenyl)ethynyl]phenyl}-4-nitrobenzamide (3o):** The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 68%; mp 167–169 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.95 (bs, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.33 (d, J = 8.8 Hz, 2H), 8.11 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.45–7.41 (m, 3H), 7.25 (d, J = 8.0 Hz, 2H), 7.16 (t, J = 7.6 Hz, 1H), 2.70 (q, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.8, 149.8, 145.9, 140.4, 138.2, 131.6, 131.3, 129.8, 128.3, 128.2, 124.3, 124.1, 119.2, 119.0, 112.8, 97.6, 83.4, 28.8, 15.2; HR-MS (ESI): m/z = 371.1395, calcd. for $C_{23}H_{19}N_2O_3$: 371.1396; anal. calcd. for $C_{23}H_{19}N_2O_3$: C 74.58, H 4.90, N 7.56; found: C 74.58, H 5.01, N 7.46.

4-Nitro-*N*-{2-[(trimethylsilyl)ethynyl]phenyl}benzamide (3p): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 85%; mp 132–134 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.94 (bs, 1H), 8.57 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.4 Hz, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H), 0.31(s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.7, 149.9, 140.2, 138.8, 131.7, 130.2, 128.2, 124.1, 124.0, 118.9, 112.3, 103.1, 100.1; HR-MS (ESI): m/z = 361.0983, calcd. for $C_{18}H_{18}N_2O_3SiNa$: 361.0986; anal. calcd. for $C_{18}H_{18}N_2O_3Si$: C 63.88, H 5.36, N 8.28; found: C 64.13, H 5.56, N 8.26.

General Procedure for the Synthesis of Arylidene-benzoxazines (4a–4o)

A mixture of the corresponding compound **3** (1.0 mmol), and iodine (10 mol%) in dry toluene (10.0 mL) was charged in a flask under an argon atmosphere and stirred for 3 days at reflux temperature. The reaction was monitered by TLC analysis. The formed product was extracted with ethyl acetate, followed by washing with water, saturated $Na_2S_2O_3$ solution and brine. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was chromatographed over silica gel using ethyl acetate:hexanes as eluent to afford the title compound.

(*Z*)-4-Benzylidene-2-phenyl-4*H*-benzo[*d*][1,3]oxazine (4a): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 95%; mp 136–138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.22 (d, J = 7.2 Hz, 2H), 7.74 (d, J = 7.2 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.55–7.22 (m, 9H), 6.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.9, 145.3, 138.9, 134.7, 131.6, 131.4, 130.4, 128.5, 128.4, 128.3, 127.8, 127.7, 126.7, 126.4, 121.8, 121.6, 101.2; HR-MS (ESI): m/z = 298.1230, calcd. for $C_{21}H_{16}NO$: 298.1232; anal. calcd. for $C_{21}H_{15}NO$: C 84.82, H 5.08, N 4.71; found: C 84.80, H 5.08, N 4.72.

(*Z*)-4-Benzylidene-2-(4-fluorophenyl)-4*H*-benzo[*d*][1,3]-oxazine (4b): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 71%; mp 120–122 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.15 (d, J = 5.6 Hz, 1H), 8.13 (d, J = 5.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 2H), 7.30–7.14 (m, 4H), 6.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 166.1, 163.6, 153.8, 145.1, 138.7, 134.6, 130.3, 130.0 (d, J = 9.1 Hz), 128.4, 128.3, 127.6 (d, J = 12.6 Hz), 126.6, 126.4, 121.8, 121.4, 115.4 (d, J = 22.0 Hz), 101.61; HR-MS (ESI): m/z = 316.1139, calcd. for $C_{21}H_{15}FNO$: 316.1138; anal. calcd. for $C_{21}H_{14}FNO$: C 79.98, H 4.47, N 4.44; found: C 78.94, H 4.43, N 4.43.

(*Z*)-4-Benzylidene-2-(4-chlorophenyl)-4*H*-benzo[*d*][1,3]-oxazine (4c): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 73%; mp 153–155 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.13 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.44–7.22 (m, 8H), 6.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.9, 145.1, 138.6, 137.8, 134.6, 130.4, 129.8, 129.1, 128.7, 128.4, 128.3, 127.9, 126.7, 126.5, 121.8, 121.5, 101.7; HR-MS (ESI): m/z = 332.0841, calcd. for $C_{21}H_{15}ClNO$: 332.0842; anal. calcd. for $C_{21}H_{14}ClNO$: C 76.02, H 4.25, N 4.22; found: C 75.91, H 4.20, N 4.20.

(*Z*)-4-Benzylidene-2-(4-nitrophenyl)-4*H*-benzo[*d*][1,3]-oxazine (4d): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 77%; mp 197–199 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.33 (d, J = 8.4 Hz, 2H), 8.28 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.44–7.25 (m, 6H), 6.23 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 152.8, 149.5, 144.8, 138.2, 137.1, 134.3, 130.6, 128.8, 128.6, 128.5, 128.4, 127.2, 126.8, 123.6, 121.9, 121.7, 102.4; HR-MS (ESI): m/z = 343.1083, calcd. for $C_{21}H_{15}N_2O_3$: 343.1081; anal. calcd. for $C_{21}H_{14}N_2O_3$: C 73.68, H 4.12, N 8.18; found: C 73.20, H 4.19, N 7.90.

(*Z*)-4-Benzylidene-2-[4-(trifluoromethyl)phenyl]-4*H*-benzo[*d*][1,3]oxazine (4e): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 54%; mp 88–90 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.0 Hz, 1H) , 7.42 (t, J = 7.2 Hz, 2H), 7.38–7.28 (m, 4H), 6.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.6, 145.0, 138.5, 134.8, 134.5, 133.1 (q, J = 33.0 Hz), 130.5, 128.5, 128.4, 128.1, 127.0, 126.7, 125.4 (q, J = 3.8 Hz),

124.0 (q, J=271.0 Hz), 121.9, 102.1; HR-MS (ESI): m/z= 366.1104, calcd. for $C_{22}H_{15}F_3NO$: 366.1106; anal. calcd. for $C_{22}H_{14}F_3NO$: C 72.32, H 3.86, N 3.83; found: C 72.01, H 3.95, N 3.79.

(*Z*)-4-Benzylidene-2-*p*-tolyl-4*H*-benzo[*d*][1,3]oxazine (4f): The title compound was prepared according to the general procedure and purified by column chromatography to afford a white solid; yield: 46%; mp 99–101 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.93 (bs, 1H), 8.62 (d, J=8.4 Hz, 1H), 7.85 (d, J=8.0 Hz, 2H), 7.56–7.38 (m, 7H), 7.27(d, J=8.0 Hz, 2H), 7.10 (td, J=8.0 Hz and 1.2 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=165.0, 142.6, 139.2, 132.0, 131.4, 131.3, 129.8, 129.5, 128.9, 128.6, 126.9, 123.4, 122.3, 119.1, 112.1, 96.8, 84.5, 21.3; HR-MS (ESI): m/z= 334.1210, calcd. for $C_{22}H_{17}NONa$: 334.1208; anal. calcd. for $C_{22}H_{17}NO$: C84.86, H 5.50, N 4.50; found: C 84.65, H 5.55, N 4.48.

(*Z*)-4-Benzylidene-2-phenyl-6-(trifluoromethyl)-4*H*-benzo[*d*][1,3]oxazine (4g): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 76%; mp 142–144 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.22 (d, J=7.2 Hz, 2H), 7.74 (d, J=7.2 Hz, 2H), 7.59 (d, J=7.6 Hz, 1H), 7.55–7.22 (m, 9H), 6.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=156.5, 144.0, 14.8, 134.0, 132.2, 130.8, 129.5 (q, J=32.6 Hz), 128.7, 128.5, 128.4, 128.1, 127.1, 129.9, 126.8 (q, J=3.8 Hz), 123.9 (q, J=277 Hz), 122.2, 119.1 (q, J=4.5 Hz), 103.5; HR-MS (ESI): m/z=298.1230, calcd. for $C_{21}H_{15}NO$: 298.1232; anal. calcd. for $C_{21}H_{14}NO$: C 84.82, H 5.08, N 4.71; found: C 84.80, H 5.08, N 4.72.

(*Z*)-4-Benzylidene-2-(4-fluorophenyl)-6-(trifluoromethyl)-4*H*-benzo[*d*][1,3]oxazine (4h): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 88%; mp 153–155 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.13 (d, J=5.2 Hz, 1H), 8.11 (d, J=5.2 Hz, 1H), 7.69 (s, 1H), 7.62 (d, J=7.2 Hz, 2H), 7.48 (d, J=8.0 Hz, 1H), 7.39 (t, J=8.0 Hz, 2H), 7.29–7.23 (m, 2H), 7.09 (t, J=8.0 Hz, 2H), 6.12 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=166.5, 164.0, 162.8, 155.5, 143.8, 141.5, 133.9, 130.4 (d, J=9.1 Hz), 129.1 (q, J=32.6 Hz), 128.5 (q, J=16.6 Hz), 126.9 (d, J=3.1 Hz), 123.2 (q, J=270.6 Hz), 122.0, 119.0 (q, J=3.8 Hz), 115.7 (d, J=22.0 Hz), 103.5; HR-MS (ESI): m/z=384.1009, calcd. for $C_{22}H_{14}F_4NO$: 384.1011; anal. calcd. for $C_{22}H_{13}F_4NO$: C 68.93, H 3.42, N 3.65; found:C 68.95, H 3.47, N 3.63.

(*Z*)-4-Benzylidene-2-(4-chlorophenyl)-6-(trifluoromethyl)-4*H*-benzo[*d*][1,3]oxazine (4i): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 73%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.13 (d, J=8.4 Hz, 2H), 7.78 (s, 1H), 7.69 (d, J=8.0 Hz, 2H), 7.56 (d, J=8.4 Hz, 1H), 7.46 (d, J=8.4 Hz, 2H), 7.42 (d, J=8.0 Hz, 2H), 7.37 (d, J=8.4 Hz, 1H), 7.29 (t, J=7.6 Hz, 1H), 6.27 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=155.7, 143.8, 138.6, 133.9, 129.5, 129.4 (q, J=11.4 Hz), 128.6, 128.5, 127.0 (q, J=3.8 Hz), 124.6 (q, J=277.6 Hz), 122.27, 119.2 (q, J=3.5 Hz), 103.7. HR-MS (ESI): m/z=400.0719, calcd. for $C_{22}H_{14}ClF_3NO$ $(M+H)^+$: 400.0716; anal. calcd. for $C_{22}H_{13}ClF_3NO$: C 66.09, H 3.28, N 3.50; found: C 65.48, H 3.33, N 3.49.

(*Z*)-2-(4-Chlorophenyl)-4-(4-fluorobenzylidene)-6-(trifluoromethyl)-4*H*-benzo[*d*][1,3]oxazine (4j): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 71%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.11 (d, J=8.8 Hz, 2H), 7.78 (s, 1H), 7.67 (dd, J=8.8 Hz and 5.6 Hz, 2H), 7.59–7.52 (m, 1H), 7.48 (d, J=8.8 Hz, 2H), 7.39 (d, J=8.4 Hz, 1H), 7.12 (t, J=8.8 Hz, 2H), 6.25 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162.8, 160.4, 147.0, 143.7, 141.5, 130.2 (d, J=8.3 Hz), 130.1, 129.3, 130.0 (d, J=24.0 Hz), 128.9, 127.2, 127.1, 124.5, 123.9, 123.6 (q, J=274 Hz), 122.1, 119.2, 119.1, 115.5 (d, J=21.2 Hz), 102.6; HR-MS (ESI): m/z= 418.0613, calcd. for $C_{22}H_{12}ClF_4NO$ $(M+H)^+$: 418.0616; anal. calcd. for $C_{22}H_{12}ClF_4NO$: C 63.25, H 2.90, N 3.35; found: C 62.92, H 3.15, N 3.25.

(*Z*)-4-(4-Fluorobenzylidene)-2-(4-nitrophenyl)-4*H*-benzo[*d*][1,3]oxazine (4k): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 76%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.33 (s, 4H), 7.67–7.64 (m, 1H), 7.60 (d, J=7.6 Hz, 2H), 7.42–7.29 (m, 3H), 7.13 (t, J=8.8 Hz, 2H), 6.23 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=162.6, 160.2, 152.7, 149.6, 144.6, 138.2, 137.1, 130.7, 130.5, 130.0 (d, J=7.6 Hz), 128.9, 128.6, 127.3, 123.7, 121.9, 121.6, 115.5 (d, J=21.2 Hz), 101.3; HR-MS (ESI): m/z=384.1009, calcd. for $C_{22}H_{14}F_4NO$: 384.1011; anal. calcd. for $C_{21}H_{13}FN_2O_3$: C 70.00, H 3.64, N 7.77; found: C 69.63, H 3.65, N 7.74.

(*Z*)-2-(4-Chlorophenyl)-4-(4-Fluorobenzylidene)-4*H*-benzo[*d*][1,3]oxazine (4l): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 70%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.12 (dt, J=8.4 Hz and 2.4 Hz, 2H), 7.69 (dd, J=8.8 Hz and 5.6 Hz, 2H), 7.58 (d, J=8.0 Hz, 1H), 7.47 (dt, J=8.4 Hz and 2.4 Hz, 2H), 7.41–7.24 (m, 4H), 7.11 (t, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C=162.5, 160.1, 153.9, 145.0, 138.4 (d, J=62.9 Hz), 130.8, 130.7, 130.6, 130.04, 129.97, 129.0 (J=22.8 Hz), 128.1, 126.9, 121.9, 121.5, 115.4 (d, J=21.2 Hz), 100.8, 29.7; HR-MS (ESI): m/z=350.0742, calcd. for $C_{21}H_{14}ONClF$ $(M+H)^+$: 350.0746; anal. calcd. for $C_{21}H_{13}ClFNO$: C 72.11, H 3.75, N 4.00; found: C 71.17, H 3.89, N, 3.86.

(*Z*)-4-(4-Fluorobenzylidene)-2-[4-(trifluoromethyl)phenyl]-4*H*-benzo[*d*][1,3]oxazine (4m): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 65%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.15–8.08 (m, 2H), 7.69–7.60 (m, 3H), 7.48 (dd, J=8.4 Hz and 1.2 Hz, 1H), 7.30 (t, J=7.6 Hz, 2H), 7.29–7.21 (m, 2H), 7.09 (t, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=166.5, 164.1, 162.8, 155.5, 143.8, 141.6, 133.9, 130.4 (d, J=9.1 Hz), 129.4 (q, J=32.6 Hz), 128.9, 128.5 (d, J=16 Hz), 126.7 (q, J=3.1 Hz), 125.0, 122.4, 122.0, 119.1 (q, J=3.8 Hz), 115.7 (d, J=22.4 Hz), 103.5; HR-MS (ESI): m/z=384.1006, calcd. for $C_{22}H_{14}ONF_4$ $(M+H)^+$: 384.1004; anal. calcd. for $C_{22}H_{13}F_4NO$: C 68.93, H 3.42, N 3.65; found: C 68.94, H 3.45, N 3.60.

(*Z*)-4-(4-Fluorobenzylidene)-2-phenyl-4*H*-benzo[*d*][1,3]-oxazine (4n): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 92%; mp 163–165 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.16 (d, J=7.2 Hz, 2H), 7.66 (dd, J=8.4 Hz and J=5.4 Hz 2H), 7.52–7.45 (m, 4H), 7.36–7.28 (m, 2H), 7.26–7.18 (m, 1H), 7.08 (t, 2H, J=

8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.4, 159.9, 154.8, 145.0, 138.8, 131.7, 131.4, 130.4, 129.9 (d, J = 7.6 Hz), 128.5, 127.8 (d, J = 5.3 Hz), 126.8, 121.8, 121.5, 115.3 (d, J = 21.2 Hz), 100.5; HR-MS (ESI): m/z = 316.1144, calcd. for $C_{21}H_{14}FNO$: 316.1142; anal. calcd. for $C_{21}H_{14}FNO$: C 79.98, H 4.47, N, 4.44; found: C 79.71, H 4.74, N 4.39.

(*Z*)-4-(4-Ethylbenzylidene)-2-(4-nitrophenyl)-4*H*-benzo[*d*][1,3]oxazine (4o): The title compound was prepared according to the general procedure and purified by column chromatography to afford a yellow solid; yield: 65%; mp 163–165 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.40 (d, J = 9.2 Hz, 2H), 8.34 (d, J = 9.2 Hz, 2H), 7.62 (t, J = 8.0 Hz, 3H), 7.40–7.27 (m, 5H), 6.26 (s, 1H), 2.71 (q, J = 8.4 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 153.0, 149.5, 144.3, 143.1, 138.2, 137.3, 131.7, 130.4, 128.8, 128.7, 128.4, 128.0, 127.1, 123.6, 122.0, 121.9, 102.5, 28.6, 15.4; HR-MS (ESI): m/z = 371.1393, calcd. for $C_{23}H_{19}N_2O_3$: 371.1396; anal. calcd. for $C_{23}H_{18}N_2O_3$: C 74.58, H 4.90, N 7.56; found: C 74.14, H 4.69, N, 7.29.

General Procedure and Characterization Data for Quinazoline 3-Oxides (8a–8o)

To a solution of benzoxazine **4** (1.0 mmol) in a mixture of dichloromethane and methanol (4:1, 10 mL) was added K_2CO_3 (10 mol%) and hydroxylamine hydrochloride (10 equiv) and the mixture stirred at room temperature for 10 h. The reaction was monitored by TLC analysis. The solvents were removed under reduced pressure and the the crude product was extracted with ethyl acetate followed by washing with water and brine and drying over anhydrous Na_2SO_4. The crude product obtained was purifed by column chromatography using a mixture of ethyl acetate and hexanes to afford the title compound.

4-Benzyl-2-phenylquinazoline 3-oxide (8a): The title compound was prepared and purified by column chromatography to afford a pale yellow solid; yield: 75%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32–8.21 (m, 2H), 8.00–7.94 (m, 2H), 7.69–7.58 (m, 2H), 7.51–7.46 (m, 4H), 7.40 (d, J = 7.2 Hz, 2H), 7.28–7.16 (m, 2H). 4.78 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 154.9, 152.9, 140.4, 135.6, 132.5, 130.7, 130.6, 130.2, 129.3, 129.2, 128.9, 128.7, 127.9, 127.8, 126.8, 123.4, 123.1; HR-MS (ESI): m/z = 313.1330, calcd. for $C_{21}H_{17}N_2O$ $(M+H)^+$: 313.1335; anal. calcd. for $C_{21}H_{17}N_2O$: C 80.75, H 5.16, N 8.97; found: C 79.84, H 5.18, N, 8.76.

4-Benzyl-2-(4-fluorophenyl)quinazoline 3-oxide (8b): The title compound was prepared and purified by column chromatography to afford a solid; yield: 51%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H = 8.42–8.40 (m, 2H), 8.04–7.90 (m, 2H), 7.76–7.60 (m, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.30–7.13 (m, 5H), 4.81 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C = 165.5, 163.0, 153.9, 153.2, 140.5, 135.6, 132.9 (d, J = 8.3 Hz), 130.9, 129.5, 129.2, 128.8 (d, J = 14.4 Hz), 127.0, 123.5, 123.2, 115.1, 114.8, 31.9; HR-MS (ESI): m/z = 331.1246, calcd. for $C_{21}H_{16}FN_2O$ $(M+H)^+$: 331.1247; anal. calcd. for $C_{21}H_{15}FN_2O$: C 76.35, H 4.58, N 8.48; found:C 76.16, H 4.69, N 8.52.

4-Benzyl-2-(4-chlorophenyl)quinazoline 3-oxide (8c): The title compound was prepared and purified by column chromatography to afford a pale yellow solid; yield: 68%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.34–8.31 (m, 2H), 8.04–7.99 (m, 2H), 7.77–7.65 (m, 2H), 7.41–7.32 (m, 2H), 7.31–7.19 (m, 5H), 4.80 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.5, 136.9, 135.5, 131.8, 131.0, 130.9, 129.6, 129.3, 129.2, 128.9, 128.8, 128.6, 128.1, 127.0, 125.3, 123.5, 123.2, 31.9; HR-MS (ESI): m/z = 331.1246, calcd. for $C_{21}H_{16}N_2O$ $(M+H)^+$: 331.1247.

4-Benzyl-2-(4-nitrophenyl)quinazoline 3-oxide (8d): The title compound was prepared and purified by column chromatography to afford a yellow solid; yield:85%; mp 170–172 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.55 (td, J = 8.8 Hz, 2.0 Hz, 2H), 8.32 (td, J = 8.8 Hz, 2.4 Hz), 8.6 (t, J = 8.4 Hz), 7.81–7.71 (m, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.31–7.20 (m, 3H), 4.81 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.7, 152.7, 148.7, 140.4, 138.6, 135.2, 131.6, 131.3, 130.4, 129.5, 128.9, 128.8, 127.1, 123.9, 123.3, 122.9, 31.9; HR-MS (ESI): m/z = 358.1191, calcd. for $C_{21}H_{16}N_3O_3$: 358.1192; anal. calcd. for $C_{21}H_{16}N_3O_3$: C 70.58, H 4.232, N 11.76; found: C 70.42, H 4.31, N 11.76.

4-Benzyl-2-[4-(trifluoromethyl)phenyl]quinazoline 3-oxide (8e): The title compound was prepared and purified by column chromatography to afford a solid; yield: 80%; mp 136–138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.44 (d, J = 8.8 Hz, 2H), 8.04 (t, J = 8.8 Hz, 2H), 7.77–7.67 (m, 4H), 7.41 (d, J = 7.6 Hz, 2H), 7.31–7.18 (m, 3H), 4.81 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.7, 153.4, 140.5, 136.0, 135.4, 132.3 (q, J = 8.1 Hz), 131.1, 130.8, 130.0, 129.4, 128.9, 128.8, 127.1, 124.8 (q, J = 15.2 Hz), 123.8, 123.3 (q, J = 271.3 Hz), 31.9; HR-MS (ESI): m/z = 381.1210, calcd. for $C_{22}H_{16}F_3N_2O$ $(M+H)^+$: 381.1209; anal. calcd. for $C_{22}H_{15}F_3N_2O$: C 69.47, H 3.97, N 7.36; found: C 69.48, H 4.02, N 7.36.

4-Benzyl-2-*p*-tolylquinazoline 3-oxide (8f): The title compound was prepared and purified by column chromatography to afford a pale yellow solid; yield: 66%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 88.23 (dt, J = 2.0 Hz and 8.4 Hz, 2H), 8.01–7.91 (m, 2H), 7.69–7.57 (m, 2H), 7.39 (d, J = 7.6 Hz, 2H), 7.32–7.161 (m, 5H), 4.78 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.0, 152.9, 141.0, 140.4, 135.7, 130.6, 130.3, 129.7, 129.1, 128.9, 128.7, 128.6, 128.5, 126.8, 123.3, 123.1, 31.8, 21.5; HR-MS (ESI): m/z = 327.1492, calcd. for $C_{22}H_{19}N_2O$ $(M+H)^+$: 327.1491; anal. calcd. for $C_{22}H_{19}N_2O$: C 80.96, H 5.56, N 8.58; found: C 79.03, H 5.52, N 8.36.

4-Benzyl-2-phenyl-6-(trifluoromethyl)quinazoline 3-oxide (8g): The title compound was prepared and purified by column chromatography to afford a solid; yield: 55%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.33–8.27 (m, 3H), 8.15 (d, J = 4.4 Hz, 1H), 7.88 (dd, J = 4.4 Hz, 1.0 Hz, 1H), 7.55–7.49 (m, 3H), 7.4 (d, J = 3.8 Hz, 2H), 7.31–7.21 (m, 4H), 4.81 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.5, 153.1, 131.9, 131.4, 130.5, 130.4, 128.9, 128.8, 128.0, 127.2, 126.3 (q, J = 6.0 Hz), 123.8 (q, J = 272.4 Hz), 122.9, 120.9 (q, J = 1.9 Hz), 32.0; HR-MS (ESI): m/z = 313.12096, calcd. for $C_{22}H_{16}F_3N_2O$ $(M+H)^+$: 381.12092; anal. calcd. for $C_{22}H_{16}F_3N_2O$: C 69.47, H 3.97, N 7.36; found: C 69.04, H 4.06, N 7.36.

4-Benzyl-2-(4-fluorophenyl)-6-(trifluoromethyl)quinazoline 3-oxide (8h): The title compound was prepared and purified by column chromatography to afford a yellow solid; yield: 81%. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.47–8.42 (m, 2H), 8.26 (t, J = 0.8 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.88 (dd, J = 2.0 Hz, 8.8 Hz, 1H), 7.40–7.37 (m, 2H), 7.31–7.15 (m, 5H), 4.79 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.8, 163.3, 155.6, 153.7, 141.1, 134.9, 133.1 (d, J = 8.3 Hz), 130.2 (q, J = 32.6 Hz), 130.4, 128.9 (d, J = 9.8 Hz), 127.9 (d, J = 3.8 Hz), 127.3, 126.4 (q, J = 3.0 Hz), 123.1 (q, J = 271.3),

122.9, 120.9 (q, $J=4.6$ Hz), 115.1 (d. $J=22.0$ Hz), 32.0; HR-MS (ESI): $m/z=399.1109$, calcd. for $C_{22}H_{15}F_4N_2O$ $(M+H)^+$: 399.1115; anal. calcd. for $C_{22}H_{15}F_4N_2O$: C 66.33, H 3.54, N 7.03; found: C 66.04, H 3.58, N 6.95.

4-Benzyl-2-(4-chlorophenyl)-6-(trifluoromethyl)quinazoline 3-oxide (8i): The title compound was prepared and purified by column chromatography to afford a pale yellow solid; yield: 36%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.36$ (dt, $J=2.4$ Hz, 9.2 Hz, 2H), 8.27 (t, $J=0.8$ Hz, 1H), 8.14 (d, $J=8.8$ Hz, 1H), 7.90 (dd, $J=1.6$ Hz, 8.8 Hz, 1H), 7.48 (dt, $J=2.4$ Hz, 9.2 Hz, 2H), 7.38 (dt, $J=1.6$ Hz, 8.4 Hz, 2H), 7.32–7.21 (m, 3H), 4.80 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=155.7$, 153.8, 141.1, 133.6 (q, $J=253.7$ Hz), 130.5, 130.3, 129.0, 128.9, 128.3, 127.3, 126.5 (q, $J=3.0$ Hz), 122.9, 120.9 (q, $J=4.5$ Hz), 120.4; anal. calcd. for $C_{22}H_{14}ClF_3N_2O$: C 63.70, H 3.40, N 6.75; found: C 63.74, H 3.65, N 6.49.

2-(4-Chlorophenyl)-4-(4-fluorobenzyl)-6-(trifluoromethyl)quinazoline 3-oxide (8j): The title compound was prepared and purified by column chromatography to afford a solid; yield: 31%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.37$–8.34 (m, 2H), 8.25 (s, 1H), 8.15 (d, $J=8.8$ Hz, 1H), 7.91 (dd, $J=1.6$ Hz, $J=8.8$ Hz, 1H), 7.50–7.47 (m, 2H), 7.39–7.34 (m, 2H), 7.01–6.95 (m, 2H), 4.74 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta_C=163.1$, 160.7, 155.6, 153.5, 141.1, 137.7, 132.0, 131.6, 131.3, 130.5(t, J=7.5 Hz), 130.1, 128.2, 126.6 (d, $J=$ 12 Hz), 122.8, 120.6 (q, $J=4.5$ Hz), 115.9, 115.7,31.2.

4-(4-Fluorobenzyl)-2-(4-nitrophenyl)quinazoline 3-oxide (8k): The title compound was prepared and purified by column chromatography to afford a solid; yield: 55%; mp 208–209 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.50$ (td, $J=$ 8.8 Hz, 2.4 Hz, 2H), 8.34 (td, $J=8.8$ Hz, 2.0 Hz, 2H), 8.10–8.01 (m, 2H), 7.83–7.74 (m, 2H), 7.40–7.36 (m, 2H), 6.97 (t, $J=8.4$ Hz, 2H), 4.77 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta_C=163.1$, 160.7, 153.1 (d, $J=69.7$ Hz), 148.8, 140.5, 138.5, 131.48 (d, $J=15.9$ Hz), 130.8, 130.6, 130.5, 130.4, 129.7, 123.7, 123.1, 122.9, 115.7 (d, $J=21.2$ Hz), 31.1; HR-MS (ESI): $m/z=376.1092$, calcd. for $C_{21}H_{14}FN_3O_3$ $(M+H)^+$: 376.1088; anal. calcd. for $C_{21}H_{14}FN_3O_3$: C 67.2, H 3.76, N 11.19; found: C 66.85, H 3.76, N 11.09.

2-(4-Chlorophenyl)-4-(4-fluorobenzyl)quinazoline 3-oxide (8l): The title compound was prepared and purified by column chromatography to afford a white solid; yield: 81%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta_H=8.34$–8.30 (m, 2H), 8.05–7.97 (m, 2H), 7.77–7.67 (m, 2H), 7.48–7.45 (m, 2H), 7.39–7.35 (m, 2H), 6.98–6.92 (m, 2H), 4.74 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=163.0$, 160.5, 153.8, 153.0, 140.4, 137.0, 131.8, 131.1, 131.0, 130.8, 130.6, 130.5, 129.7, 129.3, 128.1, 123.3, 122.9, 115.7, 115.5, 31.1; anal. calcd. for $C_{21}H_{14}ClFN_2O$: C 69.14, H 3.87, N 7.68; found: C 67.53, H 3.95, N 7.36.

4-(4-Fluorobenzyl)-2-[4-(trifluoromethyl)phenyl]quinazoline 3-oxide (8m): The title compound was prepared and purified by column chromatography to affgord an off-white solid; yield: 91%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.42$ (d, $J=8.0$ Hz, 2H), 8.05 (ddd, $J=0.8$ Hz, 8.4 Hz and 16.8 Hz, 2H), 7.81–7.71 (m, 4H), 7.41–7.38 (m, 2H), 6.96 (t, $J=$ 8.8 Hz, 2H), 4.77 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=$ 163.1, 160.6, 153.4 (d, $J=44.8$ Hz), 140.5, 135.9, 132.4 (q, $J=$ 28.6 Hz), 131.2, 130.9 (d, $J=3.0$ Hz), 130.8, 130.7, 130.6, 130.1, 129.6, 124.8 (q, $J=3.8$ Hz), 123.9 (q, $J=21.3$ Hz), 123.6, 123.1, 115.6, 31.2; anal. calcd. for $C_{22}H_{14}F_4N_2O$: C 66.35, H 3.54, N 7.03; found: C66.04, H 3.54, N 6.93.

4-(4-Fluorobenzyl)-2-phenylquinazoline 3-oxide (8n): The title compound was prepared and purified by column chromatography to afford a yellow solid; yield: 54%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.29$ (m, 2H), 8.08–8.04 (m, 1H), 7.99–7.97 (m, 1H), 7.76–7.65 (m, 2H), 7.55–7.47 (m, 3H), 7.43–7.37 (m, 2H), 6.98–6.94 (m, 2H), 4.76 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=163.0$, 160.6, 155.1, 152.8, 140.5, 132.5, 131.2 (d, $J=3.1$ Hz), 130.85 (d, $J=7.6$ Hz), 130.6 , 130.5, 130.2, 129.6, 129.4, 127.9, 123.4, 122.9, 115.6 (d, $J=21.2$ Hz), 31.2; anal. calcd. for $C_{21}H_{15}FN_2O$: C 76.35, H 4.58, N 8.48; found: C 75.04, H 5.43, N, 7.44.

4-(4-Ethylbenzyl)-2-(4-nitrophenyl)quinazoline 3-oxide (8o): The title compound was prepared and purified by column chromatography to afford a yellow solid; yield: 60%. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=88.55$ (d, $J=9.2$ Hz, 2H), 8.32 (d, $J=9.2$ Hz, 2H), 8.06 (d, $J=9.2$ Hz, 2H), 7.81–7.71 (m, 2H), 7.32 (d, $J=8.4$ Hz, 2H), 7.11 (d, $J=8.4$ Hz, 2H), 4.78 (s, 2H), 2.58 (q, $J=11.2$ Hz, 2H), 1.17 (t, $J=$ 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=153.9$, 152.7, 148.7, 143.1, 140.4, 138.6, 132.4, 131.6, 131.3, 130.3, 129.5, 128.9, 128.3, 123.9, 123.4, 122.9, 31.5, 28.4, 15.4; HR-MS (ESI): $m/z=386.1499$, calcd. for $C_{23}H_{19}N_3O_3$ $(M+H)^+$: 386.1495; anal. calcd. for $C_{23}H_{19}N_3O_3$: C 71.67, H 4.97, N 10.90; found: C 71.43, H 5.00, N 10.82.

Supporting Information

^{1}H and ^{13}C NMR spectra of all compounds are available as Supporting Information.

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