

## PAPER

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## Copper-catalyzed cross-dehydrogenative coupling between quinazoline-3-oxides and indoles†

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A novel and simple protocol for the synthesis of 4-(indole-3-yl)quinazolines *via* cross-dehydrogenative coupling of quinazoline-3-oxides and indoles under an air atmosphere has been developed. A series of biheteroaryl products were obtained in moderate to good yields.

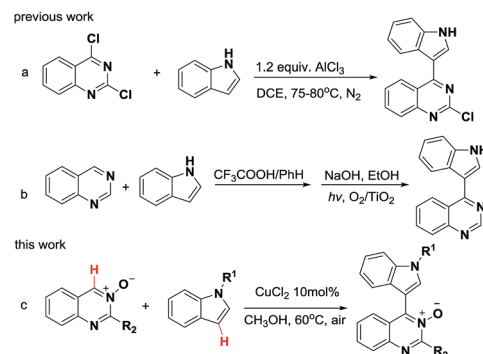
## Introduction

The nitrogen-containing heterocycles occupy an important position in pharmaceuticals and natural products.<sup>1</sup> Furthermore, they exhibit remarkable biological activities, such as anticancer, antileukemic, antiviral, and antifungal properties.<sup>2</sup> The complexity and diversity of *N*-heterocycles have been employed broadly in the studies of advanced materials and ligands for transition metal catalysis.<sup>3</sup> Among reported studies, quinazoline<sup>4</sup> and indole<sup>5</sup> derivatives are useful nitrogen-containing heterocyclic compounds, and are core structural motifs of many natural products and pharmaceuticals. Thus heterocyclic compounds bearing these two skeletons most likely possess interesting biological and physicochemical properties.<sup>6</sup> For example, indoloquinazoline derivatives have been reported to be protein kinase CK2 inhibitors<sup>6a</sup> and poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors.<sup>6b</sup> 4-(Indole-3-yl)quinazolines have been reported to be potent epidermal growth factor receptor tyrosine kinase inhibitors.<sup>6c</sup>

Over the past decade, substantial effort has been devoted to the development of reaction conditions for the coupling between quinazoline and indole compounds.<sup>7</sup> One elegant methodology relies on the nucleophilic substitution of quinazoline chlorides or their analogous with indoles. However, this method cannot be widely employed due to the need for harsh reaction conditions and/or operationally complex protocols. For instance, the substitution reaction between 2,4-dichloroquinazolines and indoles relies on 1.2 equiv. of AlCl<sub>3</sub> (Scheme 1a).<sup>7a</sup> Additionally, the reaction of quinazoline with indole required Brønsted acid mediator, followed by photocatalyzed

aromatization to give the corresponding 4-(indol-3-yl)-quinazoline product in 70% yield (Scheme 1b).<sup>7d</sup>

On the other hand, we have noticed that cross-dehydrogenative-coupling (CDC) reactions<sup>8</sup> have emerged as an excellent alternative for the formation of C–C bonds. Furthermore, the *N*-oxide moiety in aza-heteroarene compounds has been recognized as a powerful and removable directing group for *ortho* C–H bond activation.<sup>9</sup> In the past decade, pyridine *N*-oxides,<sup>10</sup> pyrimidine *N*-oxides,<sup>11</sup> quinoline *N*-oxides and isoquinoline *N*-oxides<sup>12</sup> have been extensively employed as useful building block for the preparation of a diverse range of *N*-heterocycles. However, the C4–H functionalization of quinazoline *N*-oxides remains rare.<sup>13</sup> Therefore, the development of a general and practical strategy for the synthesis of 4-(indole-3-yl)quinazolines *via* CDC reactions of quinazoline *N*-oxides and indoles under mild conditions, is highly desired. Recently, our group has directed its studies to that of the structural elaboration of quinazoline core, with the aim of constructing a quinazoline-based molecular library for bioactivity assays.<sup>14</sup> Herein, we report a copper-catalyzed CDC reaction between the Csp<sup>2</sup>–H of quinazoline-3-oxide and the Csp<sup>2</sup>–H of various indoles for the synthesis of biheteroaryl structures using a mild and operationally simple procedure (Scheme 1c).



Scheme 1 Typical strategies for the synthesis of 4-(indole-3-yl)quinazolines.

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† Electronic supplementary information (ESI) available: Experimental procedure, characterization data, <sup>1</sup>H and <sup>13</sup>C NMR spectra of compounds 3. CCDC 1813925 (compound 3ai). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8ra09864f

## Results and discussion

We initiated our investigation on the model reaction of quinazoline-3-oxide (**1a**) with *N*-methyl-indole (**2a**) in order to optimize the reaction parameters (Table 1). First, the reaction was performed in the presence of 20 mol% CuCl<sub>2</sub> at 60 °C in toluene (Entry 1). To our delight, the desired product **3a** was isolated in a moderate yield of 47%. Encouraged by this preliminary result, we then screened various solvents. The desired product was obtained in moderate or low yields when the reaction was carried out in THF, CH<sub>3</sub>CN and DMF (Entries 2–4). Further studies showed that CH<sub>3</sub>OH was the best solvent for this transformation, affording the desired product **3a** in 77% yield (Entry 7). Incrementally reducing the catalyst loading from 20 to 5 mol%, showed that 10 mol% catalyst was the optimal amount (Entries 7–9). No transformation took place in the absence of metal catalyst in CH<sub>3</sub>OH (Entry 10). Next, further screening of other metal salts was conducted, but no better conditions were discovered (Entries 11–15). Several copper salts were utilized to promote the reaction (Entries 16–20); however, it was found that copper(II) chloride was the most effective. No better result was obtained even at a higher or lower reaction temperature (Entries 21 and 22).

Table 1 Screening of the reaction condition<sup>a,b</sup>

Entry	Solvent	Catalyst	T/°C	Yield <sup>c</sup> /%
1	Toluene	CuCl <sub>2</sub> (20 mol%)	60	47
2	THF	CuCl <sub>2</sub> (20 mol%)	60	57
3	CH <sub>3</sub> CN	CuCl <sub>2</sub> (20 mol%)	60	40
4	DMF	CuCl <sub>2</sub> (20 mol%)	60	32
5	PhCl	CuCl <sub>2</sub> (20 mol%)	60	70
6	DCE	CuCl <sub>2</sub> (20 mol%)	60	75
7	CH <sub>3</sub> OH	CuCl <sub>2</sub> (20 mol%)	60	77
8	<b>CH<sub>3</sub>OH</b>	<b>CuCl<sub>2</sub> (10 mol%)</b>	<b>60</b>	<b>78</b>
9	CH <sub>3</sub> OH	CuCl <sub>2</sub> (5 mol%)	60	67
10	CH <sub>3</sub> OH	—	60	ND
11	CH <sub>3</sub> OH	In(OTf) <sub>3</sub> (10 mol%)	60	Trace
12	CH <sub>3</sub> OH	FeCl <sub>2</sub> (10 mol%)	60	37
13	CH <sub>3</sub> OH	FeCl <sub>3</sub> (10 mol%)	60	40
14	CH <sub>3</sub> OH	CoCl <sub>2</sub> (10 mol%)	60	20
15	CH <sub>3</sub> OH	Ni(OTf) <sub>2</sub> (10 mol%)	60	17
16	CH <sub>3</sub> OH	Cu(OTf) <sub>2</sub> (10 mol%)	60	73
17	CH <sub>3</sub> OH	Cu(acac) <sub>2</sub> (10 mol%)	60	Trace
18	CH <sub>3</sub> OH	CuCl (10 mol%)	60	62
19	CH <sub>3</sub> OH	CuBr (10 mol%)	60	73
20	CH <sub>3</sub> OH	Cu(OAc) <sub>2</sub> (10 mol%)	60	40
21	CH <sub>3</sub> OH	CuCl <sub>2</sub> (10 mol%)	80	53
22	CH <sub>3</sub> OH	CuCl <sub>2</sub> (10 mol%)	40	50

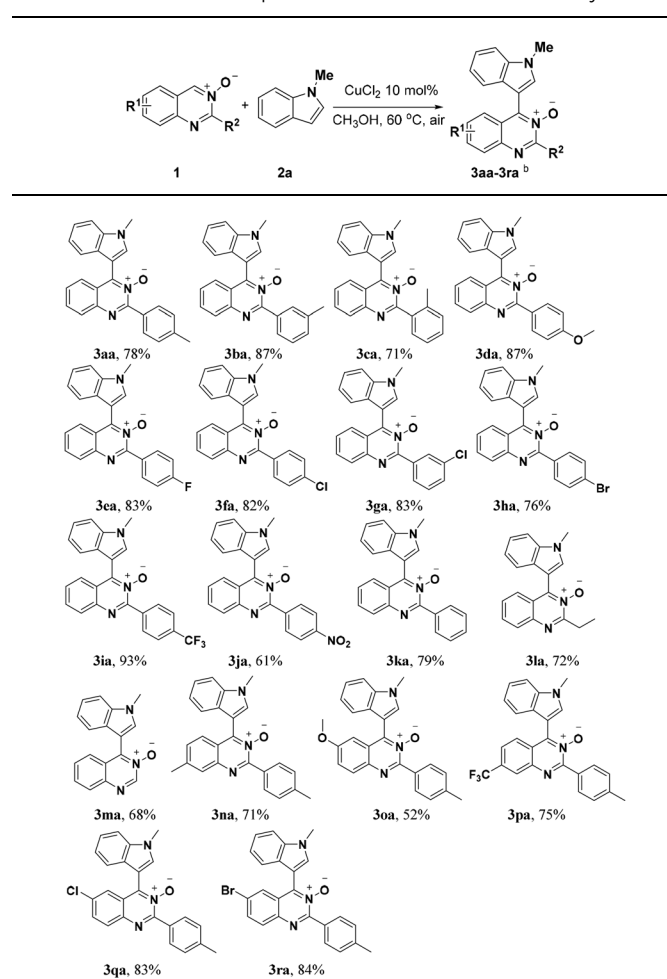
<sup>a</sup> Optimized conditions are denoted in bold. <sup>b</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst, solvent (2.0 mL), 16 h, under air.

<sup>c</sup> Isolated yield.

Under the optimized reaction conditions, the reaction scope was explored, and the results of which are shown in Table 2. The CDC reaction of quinazoline-3-oxides **1** and *N*-methylindole **2a** occurred smoothly to generate the desired products **3** in good yields. When R<sup>2</sup> was an aryl group, both electron-donating and electron-withdrawing substituents on the aryl ring had a slight effect on the reaction (**3aa–3ka**), albeit strongly electron-withdrawing substituents, such as the nitro group, greatly retarded the reaction, forming **3ja** in 61% yield. It was observed that an R<sup>2</sup> aliphatic substituent was also tolerated to give the corresponding product **3la** in 72% yield. When the parent quinazoline ring (R<sup>2</sup> = H) was used, the desired product **3ma** was obtained in 68% yield. Subsequently, R<sup>1</sup> substituents on the phenyl ring moiety of the quinazoline 3-oxide were investigated. Methyl, methoxy, trifluoromethyl, chloro and bromo functionalities were all tolerated, providing the desired products **3na–3ra** in 52–84% yields.

Subsequently, the indole scope was examined under the optimized reaction conditions. As shown in Table 3, quinazoline-3-oxide underwent smooth coupling with a variety

Table 2 The reaction of quinazoline-3-oxide **1** with 1-methylindole<sup>a</sup>



<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), CuCl<sub>2</sub> (10 mol%), CH<sub>3</sub>OH (2.0 mL), 60 °C, under air. <sup>b</sup> Isolated yield.



of substituted indoles. *N*-Methylindoles possessing alkyl, halide, and alkoxy substituents at the 5-position are amenable to the reaction conditions (**3ab–3af**), and the expected products were isolated in moderate to good yields. The coupled products were isolated in high yields for *N*-*i*Pr and *N*-Bn substrates (**3ag** and **3ah**). To our surprise, indole itself also proved to be a good coupling partner, providing the corresponding product (**3ai**) in 83% yield. Single-crystal X-ray analysis of **3ai** confirmed its structure and demonstrated the high regioselectivity of the reaction (Fig. 1). In contrast, no desired coupling product was observed for 3-methylindole, which is consistent with selectivity for the C–H activation at the 3-position of the indole (this result is not shown in Table 3). When a CH<sub>3</sub> group is present at the 2-position of the indole, the steric hindrance arising from this substituent influences the reaction; the cross-coupling product **3aj** was obtained in lower yield. However, indoles containing electron-withdrawing *N*-protecting groups, for example, *N*-tosylindole, were not amenable to this transformation, and none of the desired product (**3ak**) was isolated.

The coupled quinazoline-3-oxides products were easily deoxygenated to give the corresponding 4-(indole-3-yl)quinazolines. For example, when **3aa** was treated with PCl<sub>3</sub> (rt, 30 min), clean reduction occurred and **4a** was obtained in 86% yield (Scheme 2).<sup>15</sup> The combination of the described C–H/C–H cross-dehydrogenative-coupling and subsequent reduction provides an attractive and simple procedure for the synthesis of indole-functionalized quinazoline derivatives.

In order to further understand the mechanism of this copper-catalyzed reaction of quinazoline-3-oxide **1** with indole

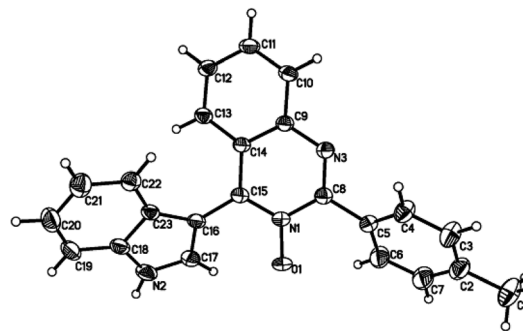


Fig. 1 X-ray ORTEP illustration of compound **3ai**.

**2**, three control experiments were conducted (Scheme 3). The desired product was obtained in 84% yield when the reaction was conducted under oxygen atmosphere (Scheme 3a). However, only a trace amount of product **3aa** was obtained when the reaction was carried out under argon, which indicates that oxygen plays a crucial role in this transformation (Scheme 3b). When **1a** was replaced by 2-(*p*-tolyl)quinazoline, the desired product was not obtained (Scheme 3c).

On the basis of these observations and related reports,<sup>16</sup> we have proposed a plausible mechanism for this reaction, as shown in Scheme 4. The CuCl<sub>2</sub> reacts with quinazoline-3-oxide **1a** to form intermediate **A** via C–H activation of **1a**. Next, **A** undergoes an insertion into the 3-position of the C–H bond of **2a** to afford **B**. Oxidation of **B** to Cu(III) complex **C** occurs via disproportionation with a second equivalent of CuCl<sub>2</sub>, liberating CuCl.<sup>17</sup> **C** undergoes reductive elimination to give the product **3aa** together with Cu(I), which is reoxidized to CuCl<sub>2</sub> by O<sub>2</sub> and HCl, to complete the cycle.

In conclusion, a novel, simple and efficient protocol for the synthesis of 4-(indole-3-yl)quinazolines via a cross-dehydrogenative coupling of quinazoline-3-oxides and indoles under an air atmosphere has been successfully developed. A series of biheteroaryl products were obtained in moderate to good yields. The unique reactivity and selectivity observed in the CDC reaction prompted us to initiate further studies on the reaction mechanism.

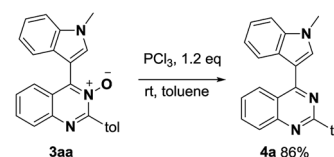
## Experimental section

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60 Å pore size, 32–63 mm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica

Table 3 The reaction of quinazoline-3-oxide **1a** with various indoles **2**<sup>a</sup>

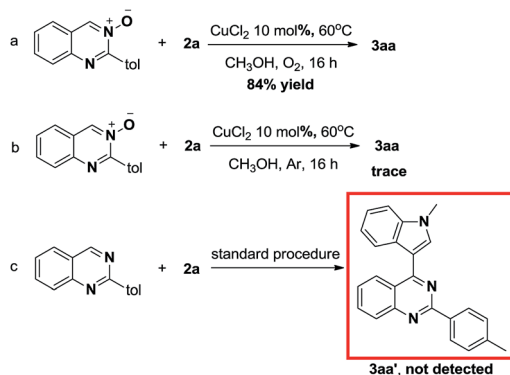
<b>1a</b>	<b>2</b>
<b>3ab</b> , 76%	<b>3ac</b> , 69%
<b>3ad</b> , 72%	<b>3ae</b> , 78%
<b>3af</b> , 87%	<b>3ag</b> , 88%
<b>3ah</b> , 82%	<b>3ai</b> , 83%
<b>3aj</b> , 58%	<b>3ak</b> , NR

<sup>a</sup> Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), CuCl<sub>2</sub> (10 mol%), CH<sub>3</sub>OH (2.0 mL), 60 °C, under air. <sup>b</sup> Isolated yield.

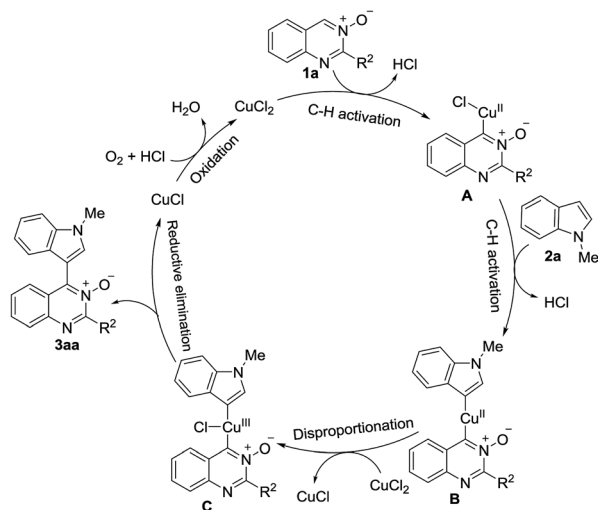


Scheme 2 Deoxygenation reaction.





Scheme 3 Control experiments.



Scheme 4 Plausible mechanism.

gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at  $\sim 20$  torr at 25–35 °C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the  $\delta$  scale.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz.

### General experimental procedure for synthesis of 3

The quinazoline-3-oxide (0.2 mmol), indole (0.3 mmol),  $\text{CuCl}_2$  (0.02 mmol) and 2.0 mL  $\text{CH}_3\text{OH}$  were mixed in a dry reaction tube. The mixture was stirred at 60 °C under air for 12–16 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated in vacuum and the residue was purified by flash column chromatography on silica gel with petroleum ether–ethyl acetate as eluent to give the desired product.

**4-(1-Methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3aa).** Compound was obtained as a yellow solid: yield 78%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (s, 1H), 8.22 (d,  $J = 8.0$  Hz, 2H), 8.04 (d,  $J = 8.0$  Hz, 1H), 7.92 (d,  $J = 8.4$  Hz, 1H), 7.69 (td,  $J = 7.6$ , 1.2 Hz, 1H), 7.52–7.40 (m, 3H), 7.36–7.27 (m, 3H), 7.19 (t,  $J = 7.6$  Hz, 1H), 3.94 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 147.1, 141.2, 140.7, 136.7, 135.5, 130.6, 130.5, 130.3, 128.7, 128.6, 128.0, 127.6, 126.5, 123.1, 122.5, 121.7, 121.0, 110.0, 102.6, 33.6, 21.6. HRMS (ESI $^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$ : 366.1606, found 366.1609.

**4-(1-Methyl-1H-indol-3-yl)-2-(m-tolyl)quinazoline 3-oxide (3ba).** Compound was obtained as a yellow solid: yield 87%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.32 (s, 1H), 8.12–7.85 (m, 3H), 7.95 (d,  $J = 8.4$  Hz, 1H), 7.71 (t,  $J = 7.2$  Hz, 1H), 7.54–7.36 (m, 4H), 7.35–7.28 (m, 2H), 7.18 (t,  $J = 7.2$  Hz, 1H), 3.95 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 147.1, 141.2, 137.5, 136.7, 135.6, 133.3, 131.2, 130.65, 130.61, 128.8, 128.1, 127.9, 127.6, 127.4, 126.6, 123.2, 122.5, 121.6, 121.0, 110.0, 102.5, 33.6, 21.5. HRMS (ESI $^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$ : 366.1606, found 366.1607.

**4-(1-Methyl-1H-indol-3-yl)-2-(o-tolyl)quinazoline 3-oxide (3ca).** Compound was obtained as a yellow solid: yield 71%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.43 (s, 1H), 8.11–8.02 (m, 2H), 7.74 (td,  $J = 7.2$ , 1.2 Hz, 1H), 7.59–7.53 (m, 2H), 7.51–7.43 (m, 2H), 7.43–7.37 (m, 1H), 7.37–7.30 (m, 3H), 7.20 (t,  $J = 7.6$  Hz, 1H), 3.92 (s, 3H), 2.35 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.8, 146.7, 140.9, 137.1, 136.8, 136.3, 134.1, 130.7, 130.2, 129.6, 128.8, 128.8, 128.3, 127.6, 126.7, 125.8, 123.2, 122.6, 121.7, 121.1, 110.1, 102.4, 33.6, 19.7. HRMS (ESI $^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}$ : 366.1606, found 366.1611.

**2-(4-Methoxyphenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3da).** Compound was obtained as a yellow solid: yield 87%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46–8.37 (m, 2H), 8.28 (s, 1H), 8.03 (d,  $J = 8.0$  Hz, 1H), 7.91 (d,  $J = 8.4$  Hz, 1H), 7.70 (td,  $J = 7.4$ , 1.2 Hz, 1H), 7.51–7.41 (m, 3H), 7.33 (t,  $J = 7.6$  Hz, 1H), 7.19 (t,  $J = 7.6$  Hz, 1H), 7.05–6.98 (m, 2H), 3.96 (s, 3H), 3.89 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.5, 155.1, 147.2, 141.3, 136.7, 135.3, 132.4, 130.6, 128.6, 127.8, 127.6, 126.5, 125.7, 123.0, 122.5, 121.7, 120.9, 113.3, 110.0, 102.7, 55.4, 33.6. HRMS (ESI $^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}_2$ : 382.1556, found 382.1555.

**2-(4-Fluorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3ea).** Compound was obtained as a yellow solid: yield 83%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.45–8.35 (m, 2H), 8.30 (s, 1H), 8.05 (d,  $J = 8.0$  Hz, 1H), 7.95 (d,  $J = 8.0$  Hz, 1H), 7.73 (t,  $J = 7.6$  Hz, 1H), 7.51 (t,  $J = 7.6$  Hz, 1H), 7.49–7.41 (m, 2H), 7.34 (t,  $J = 7.6$  Hz, 1H), 7.23–7.14 (m, 3H), 3.97 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  164.2 (d,  $J = 249.2$  Hz), 154.5, 141.2, 136.8, 135.5, 132.8 (d,  $J = 8.5$  Hz), 129.4 (d,  $J = 3.3$  Hz), 128.7, 128.2, 127.5, 126.6, 123.2, 122.6, 121.6, 121.1, 114.9 (d,  $J = 21.6$  Hz), 110.1, 102.5, 33.6. HRMS (ESI $^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{17}\text{FN}_3\text{O}$ : 370.1356, found 370.1381.

**2-(4-Chlorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3fa).** Compound was obtained as a yellow solid: yield 82%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.33 (d,  $J = 8.4$  Hz, 2H), 8.28 (s, 1H), 8.05 (d,  $J = 8.0$  Hz, 1H), 7.95 (d,  $J = 8.4$  Hz, 1H), 7.72 (t,  $J = 7.2$  Hz, 1H), 7.55–7.41 (m, 5H), 7.34 (t,  $J = 7.4$  Hz, 1H), 7.19 (t,  $J = 7.6$  Hz, 1H).





= 7.4 Hz, 1H), 3.95 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.4, 147.5, 141.2, 136.8, 136.6, 135.5, 131.9, 131.7, 130.9, 128.8, 128.3, 128.1, 127.5, 126.6, 123.2, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{17}\text{ClN}_3\text{O}$ : 386.1060, found 386.1075, and 388.1031, found 388.1044.

**2-(3-Chlorophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3ga).** Compound was obtained as a yellow solid: yield 83%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.35 (t,  $J$  = 1.6 Hz, 1H), 8.29 (s, 1H), 8.25–8.19 (m, 1H), 8.05 (d,  $J$  = 8.4 Hz, 1H), 7.95 (d,  $J$  = 8.4 Hz, 1H), 7.72 (t,  $J$  = 7.6 Hz, 1H), 7.56–7.40 (m, 5H), 7.33 (t,  $J$  = 7.4 Hz, 1H), 7.19 (t,  $J$  = 7.6 Hz, 1H), 3.95 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.1, 147.5, 141.1, 136.8, 135.5, 135.0, 133.9, 130.9, 130.5, 130.4, 129.1, 128.9, 128.6, 128.5, 127.5, 126.6, 123.3, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{17}\text{ClN}_3\text{O}$ : 386.1060, found 386.1075, and 388.1031, found 388.1045.

**2-(4-Bromophenyl)-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide 3-oxide (3ha).** Compound was obtained as a yellow solid: yield 76%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28 (s, 1H), 8.25 (d,  $J$  = 8.4 Hz, 2H), 8.05 (d,  $J$  = 8.4 Hz, 1H), 7.95 (d,  $J$  = 8.4 Hz, 1H), 7.73 (t,  $J$  = 7.4 Hz, 1H), 7.64 (d,  $J$  = 8.8 Hz, 2H), 7.52 (t,  $J$  = 7.6 Hz, 1H), 7.48–7.41 (m, 2H), 7.34 (t,  $J$  = 7.6 Hz, 1H), 7.20 (t,  $J$  = 7.4 Hz, 1H), 3.96 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.5, 147.5, 141.2, 136.8, 135.5, 132.2, 132.1, 131.1, 130.9, 128.8, 128.4, 127.5, 126.6, 125.1, 123.2, 122.6, 121.6, 121.1, 110.1, 102.4, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{17}\text{BrN}_3\text{O}$ : 430.0555, found 430.0557, and 432.0535, found 432.0537.

**4-(1-Methyl-1H-indol-3-yl)-2-(4-(trifluoromethyl)phenyl) quinazoline 3-oxide (3ia).** Compound was obtained as a yellow solid: yield 93%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.43 (d,  $J$  = 8.0 Hz, 2H), 8.31 (s, 1H), 8.07 (d,  $J$  = 8.0 Hz, 1H), 7.99 (dd,  $J$  = 8.4, 0.4 Hz, 1H), 7.77–7.73 (m, 3H), 7.55 (td,  $J$  = 7.8, 1.2 Hz, 1H), 7.46 (t,  $J$  = 8.8 Hz, 2H), 7.34 (td,  $J$  = 7.8, 1.2 Hz, 1H), 7.20 (t,  $J$  = 7.8 Hz, 1H), 3.96 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.2, 147.6, 141.2, 136.8, 135.7, 132.0 (q,  $J$  = 32.3 Hz), 131.0, 130.7, 128.9, 128.7, 127.4, 126.7, 124.8 (q,  $J$  = 3.8 Hz), 124.0 (q,  $J$  = 207.7 Hz), 123.4, 122.7, 121.6, 121.2, 110.1, 102.3, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{17}\text{F}_3\text{N}_3\text{O}$ : 420.1324, found 420.1324.

**4-(1-Methyl-1H-indol-3-yl)-2-(4-nitrophenyl)quinazoline 3-oxide (3ja).** Compound was obtained as a yellow solid: yield 61%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.58–8.50 (m, 2H), 8.38–8.29 (m, 3H), 8.08 (d,  $J$  = 8.4 Hz, 1H), 8.00 (d,  $J$  = 8.0 Hz, 1H), 7.60–7.55 (m, 1H), 7.60–7.55 (m, 1H), 7.48 (d,  $J$  = 8.4 Hz, 1H), 7.44 (d,  $J$  = 8.0 Hz, 1H), 7.77 (td,  $J$  = 7.8, 1.2 Hz, 1H), 7.58 (td,  $J$  = 7.8, 1.2 Hz, 1H), 7.48 (d,  $J$  = 8.4 Hz, 1H), 7.44 (d,  $J$  = 8.0 Hz, 1H), 7.35 (td,  $J$  = 7.6, 1.0 Hz, 1H), 7.21 (td,  $J$  = 7.6, 1.0 Hz, 1H), 3.98 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.3, 148.7, 141.3, 139.4, 136.8, 135.7, 131.5, 131.3, 129.01, 128.99, 127.4, 126.8, 123.4, 122.9, 122.8, 121.5, 121.3, 110.2, 102.2, 33.7. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{17}\text{N}_4\text{O}_3$ : 397.1301, found 397.1276.

**4-(1-Methyl-1H-indol-3-yl)-2-phenylquinazoline 3-oxide (3ka).** Compound was obtained as a yellow solid: yield 79%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.37–8.22 (m, 3H), 8.07 (d,  $J$  = 8.0 Hz, 1H), 7.96 (d,  $J$  = 8.0 Hz, 1H), 7.71 (t,  $J$  = 7.1 Hz, 1H), 7.58–7.41 (m, 6H), 7.34 (t,  $J$  = 7.2 Hz, 1H), 7.20 (t,  $J$  = 7.2 Hz, 1H), 3.95 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 147.1, 141.2, 136.7,

135.6, 133.4, 130.6, 130.4, 130.3, 128.8, 128.1, 127.9, 127.6, 126.6, 123.2, 122.5, 121.6, 121.0, 110.0, 102.5, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{18}\text{N}_3\text{O}$ : 352.1450, found 352.1437.

**2-Ethyl-4-(1-methyl-1H-indol-3-yl)quinazoline 3-oxide (3la).** Compound was obtained as a yellow solid: yield 72%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (s, 1H), 7.98 (d,  $J$  = 8.0 Hz, 1H), 7.90 (d,  $J$  = 8.4 Hz, 1H), 7.68 (t,  $J$  = 7.6 Hz, 1H), 7.51–7.41 (m, 2H), 7.38 (d,  $J$  = 8.0 Hz, 1H), 7.31 (t,  $J$  = 7.4 Hz, 1H), 7.16 (t,  $J$  = 7.4 Hz, 1H), 3.94 (s, 3H), 3.34 (q,  $J$  = 7.2 Hz, 2H), 1.53 (t,  $J$  = 7.2 Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.3, 145.8, 140.7, 136.7, 135.1, 130.4, 1228.2, 127.5, 126.5, 122.8, 122.5, 121.6, 120.9, 110.0, 102.5, 33.5, 26.3, 10.3. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}$ : 304.1450, found 304.1456.

**4-(1-Methyl-1H-indol-3-yl)quinazoline 3-oxide (3ma).** Compound was obtained as a yellow solid: yield 68%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.10 (s, 1H), 8.26 (s, 1H), 8.14–7.89 (m, 2H), 7.70 (t,  $J$  = 7.6 Hz, 1H), 7.53 (t,  $J$  = 7.6 Hz, 1H), 7.44 (d,  $J$  = 8.4 Hz, 1H), 7.39 (d,  $J$  = 8.0 Hz, 1H), 7.32 (t,  $J$  = 7.6 Hz, 1H), 7.17 (t,  $J$  = 7.4 Hz, 1H), 3.94 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  148.6, 141.5, 136.8, 135.4, 130.8, 128.8, 128.7, 127.2, 126.8, 123.2, 122.7, 121.5, 121.1, 110.1, 101.7, 33.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{17}\text{H}_{14}\text{N}_3\text{O}$ : 276.1137, found 276.1132.

**7-Methyl-4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3na).** Compound was obtained as a yellow solid: yield 71%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31 (s, 1H), 8.22 (d,  $J$  = 8.0 Hz, 2H), 7.82 (d,  $J$  = 8.8 Hz, 2H), 7.45 (dd,  $J$  = 8.6, 1.8 Hz, 2H), 7.35–7.27 (m, 4H), 7.18 (t,  $J$  = 7.6 Hz, 1H), 3.95 (s, 3H), 2.56 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 147.1, 141.6, 141.5, 140.6, 136.7, 135.5, 130.6, 130.3, 130.1, 128.5, 127.9, 127.6, 126.3, 122.4, 121.6, 121.1, 120.9, 110.0, 102.7, 33.6, 21.8, 21.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}$ : 380.1763, found 380.1767.

**6-Methoxy-4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3oa).** Compound was obtained as a yellow solid: yield 52%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.37 (s, 1H), 8.18 (d,  $J$  = 8.0 Hz, 2H), 7.95 (d,  $J$  = 9.2 Hz, 1H), 7.50–7.43 (m, 2H), 7.37–7.27 (m, 4H), 7.22–7.16 (m, 2H), 3.96 (s, 3H), 3.67 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.9, 153.6, 146.0, 140.3, 137.3, 136.7, 135.5, 130.6, 130.3, 130.1, 128.6, 127.2, 124.1, 123.2, 122.4, 121.8, 120.6, 110.1, 104.6, 102.5, 55.7, 33.6, 21.6. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}_2$ : 396.1712, found 396.1737.

**4-(1-Methyl-1H-indol-3-yl)-2-(p-tolyl)-7-(trifluoromethyl) quinazoline 3-oxide (3pa).** Compound was obtained as a yellow solid: yield 75%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.37–8.32 (m, 2H), 8.26 (d,  $J$  = 8.0 Hz, 2H), 8.06 (d,  $J$  = 8.8 Hz, 1H), 7.64 (dd,  $J$  = 8.8, 1.6 Hz, 1H), 7.47 (d,  $J$  = 8.4 Hz, 1H), 7.41 (d,  $J$  = 8.0 Hz, 1H), 7.37–7.30 (m, 3H), 7.21 (t,  $J$  = 7.6 Hz, 1H), 3.95 (s, 3H), 2.45 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.0, 147.0, 141.5, 140.2, 136.9, 136.0, 132.1 (q,  $J$  = 32.9 Hz), 130.5, 129.9, 128.8, 127.7, 127.4, 126.5 (q,  $J$  = 4.2 Hz), 124.6, 123.7 (q,  $J$  = 270.9 Hz), 123.6 (q,  $J$  = 3.0 Hz), 122.9, 121.45, 121.40, 110.3, 102.2, 33.7, 21.7. HRMS ( $\text{ESI}^+$ ):  $m/z$   $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{25}\text{H}_{19}\text{F}_3\text{N}_3\text{O}$ : 434.1480, found 434.1478.

**6-Chloro-4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3qa).** Compound was obtained as a yellow solid: yield



83%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.23 (d,  $J$  = 8.8 Hz, 3H), 7.97 (d,  $J$  = 8.8 Hz, 1H), 7.93 (d,  $J$  = 2.0 Hz, 1H), 7.62 (dd,  $J$  = 8.8, 2.0 Hz, 1H), 7.46 (d,  $J$  = 8.8 Hz, 2H), 7.47–7.29 (m, 3H), 7.22 (t,  $J$  = 7.6 Hz, 1H), 3.96 (s, 3H), 2.44 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.9, 146.3, 141.1, 139.4, 136.8, 135.3, 134.0, 131.2, 130.3, 130.1, 131.2, 130.3, 130.1, 128.6, 127.2, 125.0, 124.0, 122.7, 121.4, 121.3, 110.1, 102.3, 33.6, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{24}\text{H}_{19}\text{ClN}_3\text{O}$ : 400.1217, found 400.1219, and 402.1187, found 402.1188.

**6-Bromo-4-(1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ra).** Compound was obtained as a yellow solid: yield 84%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31–8.19 (m, 3H), 8.10 (d,  $J$  = 1.6 Hz, 1H), 7.90 (d,  $J$  = 8.8 Hz, 1H), 7.75 (dd,  $J$  = 8.8, 1.6 Hz, 3H), 7.46 (d,  $J$  = 8.4 Hz, 2H), 7.37–7.28 (m, 3H), 7.23 (t,  $J$  = 7.6 Hz, 1H), 3.96 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 146.3, 141.1, 139.7, 136.8, 135.3, 133.8, 130.34, 130.29, 130.1, 128.6, 128.3, 127.2, 124.4, 122.8, 122.0, 121.4, 121.3, 110.1, 102.3, 33.6, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{24}\text{H}_{19}\text{BrN}_3\text{O}$ : 444.0711, found 444.0706, and 446.0691, found 446.0687.

**4-(1,5-Dimethyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ab).** Compound was obtained as a yellow solid: yield 76%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.24 (s, 1H), 8.22 (d,  $J$  = 8.4 Hz, 2H), 8.05 (d,  $J$  = 8.4 Hz, 1H), 7.94 (d,  $J$  = 8.4 Hz, 1H), 7.71 (t,  $J$  = 7.6 Hz, 1H), 7.49 (t,  $J$  = 7.8 Hz, 1H), 7.34–7.30 (m, 3H), 7.22 (s, 1H), 7.14 (d,  $J$  = 8.4 Hz, 1H), 3.92 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 147.3, 141.2, 140.7, 135.4, 135.2, 130.5, 130.4, 130.3, 128.7, 128.6, 127.8, 126.6, 124.1, 123.2, 121.3, 109.7, 102.1, 33.6, 21.63, 21.57. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}$ : 380.1763, found 380.1762.

**4-(5-Methoxy-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ac).** Compound was obtained as a yellow solid: yield 69%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.29 (s, 1H), 8.27–8.18 (m, 2H), 8.05 (d,  $J$  = 8.0 Hz, 1H), 7.95 (d,  $J$  = 8.4 Hz, 1H), 7.71–7.67 (m, 1H), 7.50–7.46 (m, 1H), 7.34–7.30 (m, 3H), 6.97 (dd,  $J$  = 8.8, 2.4 Hz, 1H), 6.86 (d,  $J$  = 2.0 Hz, 1H), 3.91 (s, 3H), 3.72 (s, 3H), 2.44 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 155.1, 147.1, 141.2, 140.7, 135.8, 131.9, 130.6, 130.5, 130.3, 128.8, 128.6, 128.2, 127.7, 126.6, 122.9, 112.7, 110.7, 103.6, 102.3, 55.8, 33.7, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_2$ : 396.1712, found 396.1712.

**4-(5-Fluoro-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ad).** Compound was obtained as a yellow solid: yield 72%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.28 (s, 1H), 8.22 (d,  $J$  = 8.0 Hz, 2H), 8.06 (d,  $J$  = 8.4 Hz, 1H), 7.88 (d,  $J$  = 8.0 Hz, 1H), 7.72 (t,  $J$  = 7.4 Hz, 1H), 7.52 (t,  $J$  = 7.4 Hz, 1H), 7.38–7.35 (m, 1H), 7.31 (d,  $J$  = 7.8 Hz, 2H), 7.15–7.01 (m, 2H), 3.94 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  158.5 (d,  $J$  = 235.5 Hz), 155.7, 146.7, 141.2, 140.9, 136.6, 133.4, 130.7, 130.3, 128.9, 128.6, 128.2, 128.0 (d,  $J$  = 10.4 Hz), 126.1, 123.0, 111.2, 110.9, 110.8 (d,  $J$  = 9.8 Hz), 107.0 (d,  $J$  = 24.8 Hz), 102.8, 33.8, 29.7, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{24}\text{H}_{18}\text{FN}_3\text{O}$ : 384.1512, found 384.1501.

**4-(5-Chloro-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ae).** Compound was obtained as a yellow solid: yield 78%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (d,  $J$  = 8.4 Hz, 3H), 8.05

(d,  $J$  = 8.0 Hz, 1H), 7.84 (d,  $J$  = 8.0 Hz, 1H), 7.71 (t,  $J$  = 7.2 Hz, 1H), 7.52 (t,  $J$  = 7.2 Hz, 1H), 7.42 (s, 1H), 7.36–7.25 (m, 4H), 3.92 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 146.5, 141.2, 140.9, 136.2, 135.2, 130.8, 130.3, 128.9, 128.6, 128.5, 128.3, 127.0, 126.0, 123.1, 123.0, 121.1, 111.0, 102.4, 33.7, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{24}\text{H}_{18}\text{ClN}_3\text{O}$ : 400.1217, found 400.1219, and 402.1187, found 402.1188.

**4-(5-Bromo-1-methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3af).** Compound was obtained as a yellow solid: yield 87%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22 (d,  $J$  = 8.0 Hz, 1H), 8.19 (s, 1H), 8.05 (d,  $J$  = 8.4 Hz, 1H), 7.83 (d,  $J$  = 8.0 Hz, 1H), 7.71 (t,  $J$  = 6.8 Hz, 1H), 7.57 (s, 1H), 7.52 (t,  $J$  = 7.2 Hz, 1H), 7.40 (d,  $J$  = 8.4 Hz, 1H), 7.31 (d,  $J$  = 8.0 Hz, 3H), 3.92 (s, 3H), 2.43 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 146.5, 141.2, 140.9, 136.1, 135.5, 130.8, 130.3, 129.1, 128.9, 128.6, 128.3, 126.0, 125.5, 124.1, 123.1, 114.5, 111.5, 102.4, 100.0, 33.7, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{23}\text{H}_{18}\text{BrN}_3\text{O}$ : 444.0711, found 444.0710, and 446.0691, found 446.0690.

**4-(1-Isopropyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ag).** Compound was obtained as a yellow solid: yield 88%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.46 (s, 1H), 8.19 (d,  $J$  = 8.0 Hz, 2H), 8.05 (d,  $J$  = 8.0 Hz, 1H), 7.94 (d,  $J$  = 8.4 Hz, 1H), 7.70 (t,  $J$  = 7.4 Hz, 1H), 7.56–7.44 (m, 3H), 7.36–7.28 (m, 3H), 7.18 (t,  $J$  = 7.4 Hz, 1H), 4.90–4.75 (m, 1H), 2.44 (s, 3H), 1.67 (s, 3H), 1.65 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.9, 147.4, 141.3, 140.6, 135.7, 131.0, 130.61, 130.55, 130.2, 128.7, 128.6, 127.9, 127.8, 126.7, 123.2, 122.2, 121.9, 120.9, 110.3, 102.8, 48.1, 22.8, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{26}\text{H}_{24}\text{N}_3\text{O}$ : 394.1919, found 394.1919.

**4-(1-Benzyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ah).** Compound was obtained as a yellow solid: yield 82%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.33 (s, 1H), 8.22 (d,  $J$  = 7.6 Hz, 2H), 8.04 (d,  $J$  = 8.4 Hz, 1H), 7.92 (d,  $J$  = 8.4 Hz, 1H), 7.68 (t,  $J$  = 7.4 Hz, 1H), 7.47 (t,  $J$  = 8.2 Hz, 2H), 7.40 (d,  $J$  = 8.0 Hz, 1H), 7.37–7.21 (m, 7H), 7.17 (t,  $J$  = 7.4 Hz, 1H), 5.45 (s, 2H), 2.42 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.8, 147.0, 141.1, 140.7, 136.3, 134.8, 130.53, 130.47, 130.3, 129.0, 128.8, 128.6, 128.1, 128.0, 127.2, 126.4, 123.2, 122.6, 121.9, 121.1, 110.6, 103.4, 51.0, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{30}\text{H}_{24}\text{N}_3\text{O}$ : 442.1919, found 442.1935.

**4-(1H-Indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3ai).** Compound was obtained as a yellow solid: yield 83%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  10.24 (s, 1H), 8.28 (d,  $J$  = 7.2 Hz, 2H), 8.05 (d,  $J$  = 8.4 Hz, 1H), 7.77 (d,  $J$  = 8.4 Hz, 1H), 7.71 (t,  $J$  = 7.2 Hz, 1H), 7.57–7.39 (m, 3H), 7.33 (d,  $J$  = 7.6 Hz, 2H), 7.08 (s, 3H), 2.44 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 148.5, 141.5, 140.9, 136.1, 131.1, 131.0, 130.5, 130.4, 128.7, 128.6, 128.3, 126.6, 126.3, 123.5, 122.4, 121.4, 120.8, 112.3, 103.5, 21.6. HRMS (ESI $^+$ ):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  calcd for  $\text{C}_{23}\text{H}_{18}\text{N}_3\text{O}$ : 352.1450, found 352.1447.

**4-(2-Methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline 3-oxide (3aj).** Compound was obtained as a yellow solid: yield 58%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.55 (s, 1H), 8.31 (d,  $J$  = 8.0 Hz, 2H), 8.06 (d,  $J$  = 8.4 Hz, 1H), 7.69 (t,  $J$  = 7.6 Hz, 1H), 7.56 (d,  $J$  = 8.4 Hz, 1H), 7.44 (t,  $J$  = 7.6 Hz, 1H), 7.32 (d,  $J$  = 8.0 Hz, 2H), 7.18 (d,  $J$  = 7.7 Hz, 1H), 7.05 (s, 3H), 2.43 (s, 3H), 2.04 (s, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 149.4, 141.03, 140.99, 139.7,



136.1, 130.8, 130.50, 130.45, 128.7, 128.5, 127.7, 126.6, 124.2, 121.4, 120.2, 119.5, 111.7, 101.3, 21.6, 13.7. HRMS (ESI):  $m/z$   $[M + H]^+$  calcd for  $C_{24}H_{20}N_3O$ : 366.1606, found 366.1602.

#### 4-(1-Methyl-1H-indol-3-yl)-2-(p-tolyl)quinazoline (4a).

Compound was obtained as an off-white solid: yield 86%;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.64 (d,  $J = 8.4$  Hz, 2H), 8.37 (d,  $J = 8.4$  Hz, 2H), 8.11 (d,  $J = 8.4$  Hz, 1H), 7.85 (td,  $J = 7.0, 1.2$  Hz, 1H), 7.76 (s, 1H), 7.53 (td,  $J = 7.6, 0.8$  Hz, 1H), 7.45 (d,  $J = 7.6$  Hz, 1H), 7.42–7.31 (m, 4H), 3.94 (s, 3H), 2.46 (s, 3H).  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  163.1, 160.4, 152.1, 140.4, 137.6, 136.1, 133.0, 132.7, 129.3, 129.1, 128.6, 127.4, 126.8, 126.3, 123.0, 122.1, 121.8, 121.4, 113.4, 109.7, 33.4, 21.54. HRMS (ESI):  $m/z$   $[M + H]^+$  calcd for  $C_{24}H_{19}N_3$ : 350.1657, found 350.1656.

## Conflicts of interest

There are no conflicts to declare.

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