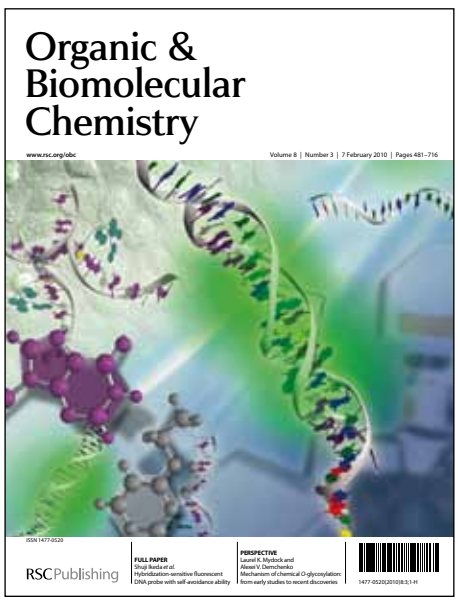
Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: Y. Peng, H. Lu, Q. Yang, Y. Zhou, Y. Guo, Z. Deng and Q. Ding, *Org. Biomol. Chem.*, 2013, DOI: 10.1039/C3OB41955J.



This is an *Accepted Manuscript*, which has been through the RSC Publishing peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, which is prior to technical editing, formatting and proof reading. This free service from RSC Publishing allows authors to make their results available to the community, in citable form, before publication of the edited article. This *Accepted Manuscript* will be replaced by the edited and formatted *Advance Article* as soon as this is available.

To cite this manuscript please use its permanent Digital Object Identifier (DOI®), which is identical for all formats of publication.

More information about *Accepted Manuscripts* can be found in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics contained in the manuscript submitted by the author(s) which may alter content, and that the standard **Terms & Conditions** and the **ethical guidelines** that apply to the journal are still applicable. In no event shall the RSC be held responsible for any errors or omissions in these *Accepted Manuscript* manuscripts or any consequences arising from the use of any information contained in them.

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

View Article Online
DOI: 10.1039/C3OB41955J
ARTICLE TYPE

Cross-Coupling/Annulations of Quinazolones with Alkynes for Access to Fused Polycyclic Heteroarenes under Mild Conditions

Hui Lu,[b] Qin Yang,[a] Yirong Zhou,[a] Yanqin Guo,[a] Zhihong Deng,[b] Qiuping Ding,[b] and Yiyuan peng*[a,b]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

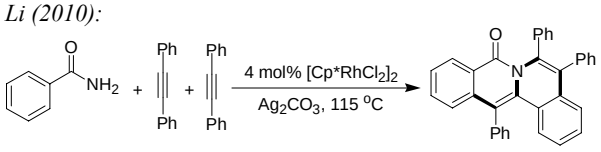
Ruthenium-catalyzed regioselective oxidative cross-coupling/annulations of quinazolones with alkynes were successfully developed for direct access to fused polycyclic heteroarenes. The transformation proceeded well with a broad substrate scope under mild conditions to accomplish in moderate to high yields.

Introduction

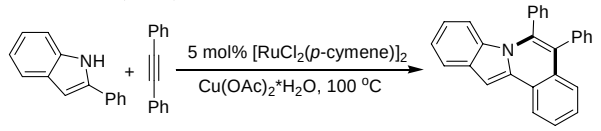
In the last few decades, transition metal-catalyzed C-H bond activation for the construction of C-C bond proved to be the most direct and efficient preparation of complex chemical compounds in an atom- and step-economic manner.[1] Undoubtedly, rhodium (Rh) catalyst was the most widely used one to promote the oxidative coupling/cyclization sequence via C-H bound activation. A variety of directing groups have been successfully induced for various cheating assistant Rh-mediated dehydrogenative annulations processes.[2] General functional groups containing oxygen or nitrogen atoms like carboxylic acid,[3] carbonyl of ketone,[4] phenolic hydroxyl,[5] imine,[6] oxime,[7] benzamide,[8] benzhydroxamic acid,[9] hydroxamic acid,[10] amide,[11] acetanilide,[12] acrylamide,[13] enamine,[14] urea,[15] azide[16] and some small heterocyclics[17] including azole, benzimidazole, imidazole, benzoxazole, indole and pyridine etc, all served as potential directing groups. Very recently, a much less expensive ruthenium (Ru) catalyst has been employed by Ackermann et al. to replace Rh catalyst for many similar processes.[18]

At the same time, fused polycyclic heteroaromatic frameworks bearing one or more nitrogen atoms have attracted significant attention for theirs unique biological and photo-electrochemical properties.[19] However, the traditional synthetic routs were long and usually required costly complicated operations. Recently, the transition metal mediated C-H functionalizations have become an alternative and partially circumvented the existing shortcomings. Moreover, alkynes have been lately found extensive applications in various catalytic tandem sequential transformations to access multicyclic structures.[2-18,20] Our group is always interesting in the synthesis of quinazoline derivatives[21] and we anticipated that quinazolinones core structure may participate the catalytic tandem reactions with alkynes because it containing an amide moiety which have been proven to be effective directing group (scheme 1).[18e,20] Herein, we present a useful ruthenium-catalyzed oxidative cross-coupling/annulations between quinazolones and alkynes for facile access to fused polycyclic heteroarenes in regioselective fashion under mild conditions.

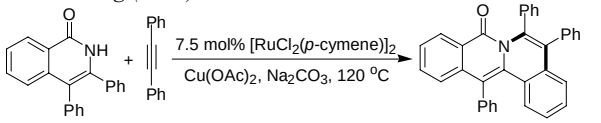
Li (2010):



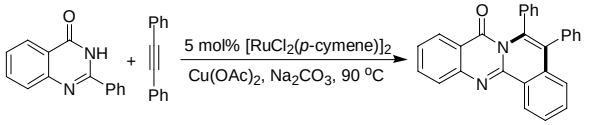
Ackermann (2012):



Li and Wang (2012):



This work:



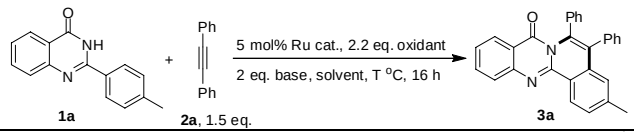
Scheme 1 Recent Examples of Amide Directing Transition Metal-catalyzed Oxidative Coupling/Annulations of Alkynes.

Results and discussion

As an initial attempt, 2-*p*-tolyl-4-quinazolinone (**1a**) was treated with diphenylacetylene (**2a**) in the presence of Ru catalyst (5 mol% $[RuCl_2(p\text{-cymene})]_2$), oxidant (2.2 equiv of $Cu(OAc)_2$) and base (2.0 equiv of Na_2CO_3) in PhCl at 90 °C under N_2 atmosphere for 16 hours. To our delight, the reaction proceed clear to isolate **3a** in 82% yield (Table1, entry 1). The structure of **3a** was comfirmed by X-ray diffiraction analysis (see the Surpporting Informatiom). When the reaction was performed in air under identical conditions, the yield did not fluctuate (Table1, entry 1). This result indicated that the atmosphere did not exert

any influence on the transformation. The following optimization of reaction parameters were all conducted systematically under air for simple experimental operation. Firstly, the solvent effects were investigated (see the Surpporting Informatiom for detailed information). When toluene was used, the yield increased to 92% (Table1, entry 2). While halogenated solvent DCE provided moderate yield of 75% (see the Surpporting Informatiom for detailed information). The further examination including some aprotic polar solvent, such as THF, DMF, NMP and MeCN all delivered inferior outcomes. Protic MeOH was also examined and generated low efficiency (see the Surpporting Informatiom for detailed information). So, aromatic solvent toluene was chosen as the optimal solvent for further optimization. Next, a group of oxidants like copper salts and silver salts were screened (see the Surpporting Informatiom for detailed information). The counter anion played significant role in the process. Only acetate could enhance the catalytic activity while others turned out to be unsuitable, thereby in agreement with literature description of carboxylate assistance for the transition metal-catalyzed C-H functionalizations. Then, both inorganic and organic base were evaluated as additive (see the Surpporting Informatiom for detailed information). Only K_3PO_4 could afford good yield of 79%, while other inorganic bases including K_2CO_3, Cs_2CO_3, NaOH, and t-BuOK all gave moderate yield. On the other hand, among the organic bases, triethylamine generated the highest yield of 85%, While DBU and DABCO just provided lower yields. Finally, the reaction temperature was also investigated for its well-known significant influence on the reaction rate. Higher or lower temperature seemed to be not appropriate for the transformation because decreased yields were generated in such cases (Table1, entries 6 and 7).

Table 1. Optimization of Reaction Conditions[a]

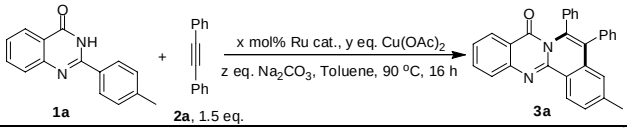


entry	solvent	oxidant	base	T (°C)	yield (%)[b]
1[c]	PhCl	$Cu(OAc)_2$	Na_2CO_3	90	81(82)[c]
2	Toluene	$Cu(OAc)_2$	Na_2CO_3	90	92
3	Toluene	AgOAc	Na_2CO_3	90	87
4	Toluene	$Cu(OAc)_2$	Et_3N	90	85
5	Toluene	$Cu(OAc)_2$	Na_2CO_3	120	67
6	Toluene	$Cu(OAc)_2$	Na_2CO_3	60	87
7	Toluene	$Cu(OAc)_2$*H_2O	Na_2CO_3	90	86

[a] The reaction was carried out on a 0.2 mmol of **1a** with 1.5 equiv of **2a** in presence of 5 mol% catalyst $[RuCl_2(p\text{-cymene})]_2$, 2.2 equiv of oxidant and 2.0 equiv of base additive in 3 mL solvent at indicated temperature for 16 hours. [b] Isolated yield. [c] The data in parentheses was obtained under N_2 atmosphere reaction condition.

Encouraged by the above preliminary results, we continued to investigate the catalyst and reagent loading's effects on the catalytic process. The results are summarized in Table 2. The yield decreased sharply accompany by a reduction of the catalyst loading, oxidant loading or base loading (Table 2, entries 1, 4 and 6). On the other hand, when the dose of the three reagents increased, the yield did not raise anymore (Table 2, entries 3, 5 and 7). Additionally, the control experiments shown that in absence of any one of the reaction parameters or reagents, the reaction could not proceed anymore. Furthermore, several other kinds of ruthenium catalysts, such as $Ru(PPh_3)Cl_2$, $[Ru(bipy)_3]Cl_2$*$6H_2O$, $Ru(COD)Cl_2$ and $RuCl_3$*H_2O were also examined, but only trace amount expected product were detected.

Table 2. Catalyst and Reagent Loading Screening[a]

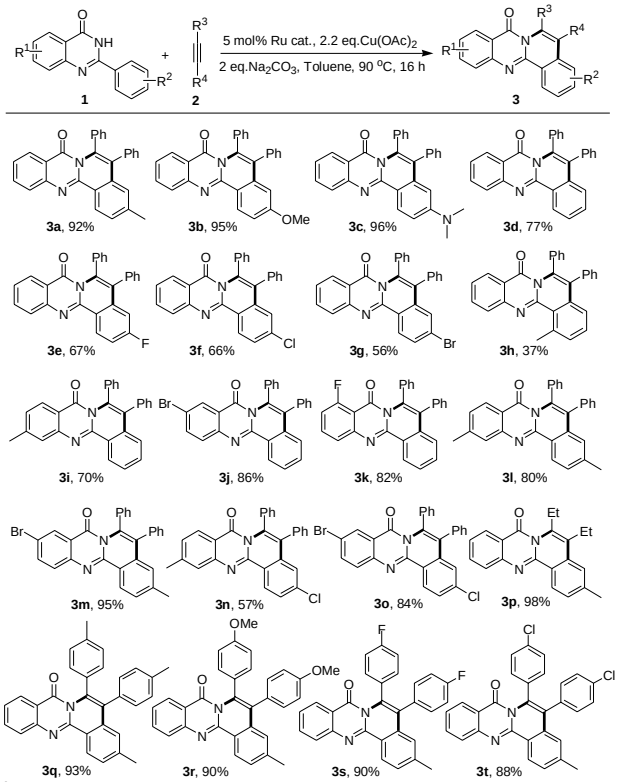


entry	Ru catalyst (x mol%)	$Cu(OAc)_2$ (y equiv)	Na_2CO_3 (z equiv)	yield (%)[b]
1	2.5	2.2	2.0	54
2	5.0	2.2	2.0	92
3	7.5	2.2	2.0	93
4	5.0	1.2	2.0	52
5	5.0	3.2	2.0	92
6	5.0	2.2	1.5	69
7	5.0	2.2	2.5	92

[a] The reaction was carried out on a 0.2 mmol of **1a** with 1.5 equiv of **2a** in presence of x mol% catalyst $[RuCl_2(p\text{-cymene})]_2$, y equiv of $Cu(OAc)_2$ and z equiv of Na_2CO_3 in 3 mL toluene at 90 °C for 16 hours. [b] Isolated yield.

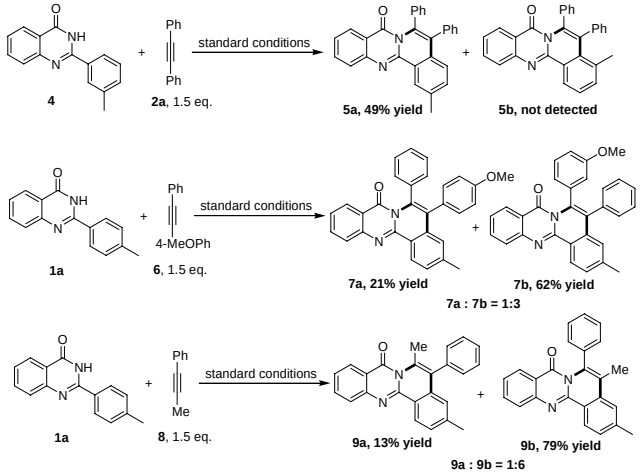
With the optimized reaction conditions in hand, the substrate scope was explored. As illustrated in Table 3, a wide range of quinazolinones and alkynes could be well tolerated in our catalytic system. Different substituents on the 2-position benzene ring were firstly probed (**3a**-**3h**). The substrates bearing electronic-donor substitutions generally afforded better outcomes than electronic-withdrawing ones. It was noteworthy that the halo atoms could be tolerant under the identical conditions albeit with moderate yields. Nevertheless, when the 2-position of the benzene ring was substituted by methyl group on 2`-position (**3h**), the yield sharply decreased to 37% along with 56% starting material **1h** recovered, probably due to the big steric hindrance. After finishing the above examination, we moved on to check the mother aromatic ring of the quinazolinone. The opposite influence of the electronic properties on the catalytic transformation was observed this time. Unlike the previous results, the electro-deficient quinazolinones all produced higher yields than electro-rich ones no matter what the situations of 2-position substituted benzene ring were (**3i**-**3o**). Subsequently, different symmetric internal alkynes were also assessed. Gratifyingly, both the alkyl and aryl alkynes could react smoothly with quinazolinone **1a** to provide the expect product in high yields (**3p**-**3t**). Notably, diethyl acetylene generated the best result to give almost quantitative yield of **3p**.

Table 3. Substrate Scope Exploration[a]



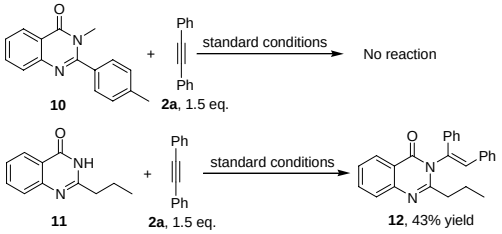
[a]The reaction was carried out on a 0.2 mmol of **1a** with 1.5 equiv of **2a** in presence of 5 mol% catalyst $[RuCl_2(p\text{-cymene})]_2$, 2.2 equiv of $Cu(OAc)_2$ and 2 equiv of Na_2CO_3 in 3 mL toluene at 90 °C for 16 hours. Isolated yield.

Additionally, the regioselectivities were evaluated by the employment of 3`-position of benene ring substituted substrate **4** and unsymmetric alkynes **6** and **8** (scheme 2). In case of **4**, only single regioisomer **5a** was detected probably caused by the steric hindrance difference. However, while unsymmetric alkynes **6** and **8** were ultilized, the moderate regioselectivities of 3:1 and 6:1 ratio were obtained, respectively. The structure of **7b** and **9b** were also comfirmed by X-ray diffiraction analysis (see the Surpporting Informatiom).



Scheme 2 Evaluation of the Regioselectivity.

Moreover, some preliminary investigations were further carried out for better understanding the details of the exact reaction mechanism (scheme 3). When the directing group amide was blocked by methyl group (**10**), the reaction could not proceed anymore. It meant the directing group was a pivotal element for the transition metal catalytic transformation. Then, when the 2-position aromatic ring was replaced by alkyl chain, the much more challenged sp^3 C-H bond activation did not occur. However, 2-propyl substituted quinazolinone **11** underwent the coupling with diphenylacetylene (**2a**) via the N-H bond cleavage to provide the product **12** in moderate yield. This phenomenon indicated that the N-H bond could be functionalized solely without the participation of the C-H bond activation.



Scheme 3 Preliminary Investigation of the Reaction Mechanism.

Conclusions

In summary, we have demonstrated an unprecedented ruthenium-catalyzed regioselective oxidative cross-coupling/cyclizations of quinazolones with alkynes for the facile construction of fused tetracyclic heteroarenes. The transformation proceeded well with a broad substrate scope under mild conditions to accomplish in moderate to high yields. Moreover, the preliminary investigations of the reaction mechanism showed that the N-H bond could be functionalized solely without the C-H bond cleavage. Further more work is currently underway in our laboratory for better understanding of the exact reaction pathway.

Experimental Section

All reactions were performed in reaction tubes under air. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 μm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica 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 ~20 Torr (house vacuum) at 25–35°C. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General experimental procedure for synthesis of **3**. A mixture of quinazolinone (**1**) (0.2mmol, 1.0eq), the alkyne (**2**) (0.3mmol, 1.5eq), $[RuCl_2(p\text{-cymene})]_2$ (5%), Na_2CO_3 (0.4mmol, 2.0eq), $Cu(OAc)_2$ (0.44mmol, 2.2eq), toluene (2ml) were added to a reaction tube. The mixture was stirred at 90 °C for 16 hours. Afterwards, it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel.

View Article Online
DOI: 10.1039/C3OB41955J

3-methyl-5,6-diphenyl-8H-isoquinolino[1,2-b]quinazolin-8-one (**3a**). White solid (yield 92%), mp: 264-265 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.78 (t, J = 7.2 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 7.2 Hz, 1H), 7.27-7.23 (m, 3H), 7.10-7.05 (m, 7H), 6.95 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 147.7, 147.0, 142.7, 137.2, 135.6, 135.3, 134.4, 133.9, 131.2, 129.8, 128.5, 128.0, 127.7, 127.2, 127.2, 126.8, 126.7, 126.2, 125.4, 124.9, 120.1, 22.0; HRMS (ESI) calcd. for $C_{29}H_{20}KN_2O$ ($M + K^+$), 451.1213; Found, 451.1224; IR (cm^{-1}) v 2922, 1706, 1599, 1541, 1487, 1444, 1292, 1155, 822, 770, 694.

3-methoxy-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3b**)**.** White solid (yield 95%), mp: 246-247 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, J = 8.8 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.84-7.76 (m, 2H), 7.73-7.70 (m, 1H), 7.54- 7.51 (m, 1H), 7.35 (t, J = 6.8 Hz, 1H), 7.28- 7.22 (m, 1H), 7.19 (d, J = 8.8 Hz, 1H), 7.13-7.11 (m, 3H), 7.08-7.05 (m, 4H), 6.57 (d, J = 6.4 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 161.4, 147.5, 147.2, 137.1, 135.9, 135.5, 134.4, 131.1, 129.3, 128.5, 128.1, 127.6, 127.3, 127.2, 127.2, 126.9, 126.5, 125.1, 120.7, 119.8, 116.3, 109.0, 55.4; HRMS (ESI) calcd. for $C_{29}H_{20}N_2NaO_2$ ($M + Na^+$), 451.1422; Found, 451.1440; IR (cm^{-1}) v 2918, 1700, 1608, 1541, 1492, 1461, 1285, 1236, 857, 761, 702.

3-(dimethylamino)-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3c**). Yellow solid (yield 96%), mp: 278-279 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 9.2 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.79-7.71 (m, 3H), 7.52-7.51 (m, 1H), 7.31-7.22 (m, 3H), 7.10-6.97 (m, 6H), 6.98 (d, J = 8.8 Hz, 1H), 6.19 (s, 1H), 2.88 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 152.6, 148.2, 147.7, 137.6, 136.1, 135.6, 134.2, 132.3, 131.1, 130.9, 128.9, 128.7, 128.5, 127.9, 127.2, 127.1, 126.6, 126.2, 124.2, 119.5, 116.0,113.5, 106.6, 39.1; HRMS (ESI) calcd. for $C_{30}H_{24}N_3O$ ($M + H^+$), 442.1919; Found, 442.1920; IR (cm^{-1}) v 2960, 1728, 1608, 1537, 1492, 1467, 1290, 1124, 842, 778, 698.

5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3d**). White solid (yield 77%), mp: 261-262 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, J = 7.6 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 6.8 Hz, 1H), 7.62 (t, J = 6.8 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 6.8 Hz,1H), 7.25 (m, 3H), 7.18 (d, J = 7.6 Hz, 1H), 7.12-7.07 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 147.5, 146.9, 137.0, 135.5, 135.2, 134.5, 133.9, 132.0, 131.2, 128.5, 128.3, 128.0, 127.8, 127.3, 127.2, 127.1, 126.9, 126.8, 126.2, 125.6, 120.3; HRMS (ESI) calcd. for $C_{28}H_{19}N_2O$ ($M + H^+$), 399.1497; Found, 399.1506; IR (cm^{-1}) v 2930, 1697, 1607, 1546, 1487, 1468, 1298, 1137, 768, 696.

3-fluoro-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3e**). White solid (yield 67%), mp: 247-248 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, J = 9.2 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.87-7.82 (m, 2H), 7.41 (t, J = 6.8 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.35-7.36 (m, 3H), 7.14-7.06 (m, 7H), 6.84 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1 (d, $^1J_{CF}$ = 252 Hz), 161.2, 146.9, 146.8, 136.7, 136.6, 136.3 (d, $^3J_{CF}$ = 10 Hz), 135.0, 134.6, 131.0, 130.3, 130.2, 128.4, 128.3, 127.6, 127.2, 127.1, 127.0, 126.7, 125.7, 123.7, 120.1, 116.6 (d, $^2J_{CF}$ = 23 Hz),111.9 (d, $^2J_{CF}$ = 23 Hz); HRMS (ESI) calcd. for $C_{28}H_{18}FN_2O$ ($M + H^+$), 417.1403; Found: 417.1423; IR (cm^{-1}) v 2919, 1704, 1613, 1549, 1489, 1469, 1292, 1202, 863, 766, 695.

3-chloro-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3f**). White solid (yield 66%), mp: 236-237 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.84-7.77 (m, 2H), 7.53 (d, J = 8.4Hz, 1H), 7.39 (t, J = 6.8 Hz, 1H), 7.26 (m, 3H), 7.12-7.06 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 146.8, 146.7, 138.6, 136.7, 136.6, 135.3, 134.8, 134.6, 131.1, 128.9, 128.7, 128.4, 128.3, 127.6, 127.2, 127.1, 126.8, 126.6, 125.9, 125.7, 125.6, 120.2; HRMS (ESI) calcd. for $C_{28}H_{18}ClN_2O$ ($M + H^+$), 433.1108; Found: 433.1115; IR (cm^{-1}) v 2959, 1701, 1613, 1549, 1488, 1469, 1292, 1117, 863, 775, 695.

3-bromo-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3g**). White solid (yield 56%), mp: 223-224 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.85-7.78 (m, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.40 (t, J = 6.8 Hz, 1H), 7.29-7.27 (m, 4H), 7.13-7.05 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 147.0, 146.7, 136.7, 136.6, 135.5, 134.7, 134.6, 131.6, 131.0, 128.9, 128.7, 128.4, 128.3, 127.6, 127.2, 127.1, 126.8, 126.5, 126.1, 125.9, 120.3; HRMS (ESI) calcd. for $C_{28}H_{18}BrN_2O$ ($M + H^+$), 477.0603; Found: 477.0597; IR (cm^{-1}) v 2930, 1712, 1604, 1544, 1479, 1330, 1288, 1175, 868, 744, 702.

1-methyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3h**). White solid (yield 37%), mp: 226-227 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 7.2 Hz, 1H), 7.44-7.37 (m, 3H), 7.26-7.24 (m, 3H), 7.09-7.06 (m, 8H), 3.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 148.3, 146.2, 141.1, 137.0, 136.3, 135.6, 134.9, 134.2, 132.7, 131.3, 130.8, 128.5, 128.0, 127.2, 127.0, 126.9, 125.8, 125.7, 124.8, 120.1, 27.2; HRMS (ESI) calcd. for $C_{29}H_{20}N_2NaO$ ($M + Na^+$), 435.1473; Found, 435.1486; IR (cm^{-1}) v 2926, 1689, 1606, 1552, 1490, 1443, 1282, 1139, 802, 764, 701.

11-methyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3i**). White solid (yield 70%), mp: 251-252 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, J = 7.6 Hz, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.72-7.67 (m, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.56-7.52 (m, 2H), 7.25-7.18 (m, 3H), 7.17 (d, J = 7.6 Hz, 1H), 7.11-7.07 (m, 6H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 147.6, 146.9, 145.4, 137.1, 135.6, 133.9, 132.3, 131.8, 131.1, 130.9, 128.8, 128.4, 128.2, 128.0, 127.4, 127.3, 127.2, 127.1, 127.0, 126.8, 126.4, 126.1, 117.9, 22.0; HRMS (ESI) calcd. for $C_{29}H_{20}N_2NaO$ ($M + Na^+$), 435.1473; Found, 435.1464; IR (cm^{-1}) v 2960, 1690, 1610, 1544, 1483, 1442, 1282, 1074, 790, 700.

10-bromo-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3j**). White solid (yield 86%), mp: 230-231 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, J = 8.0 Hz, 1H), 8.26 (s, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.61-7.54 (m, 2H), 7.26-7.25 (m, 3H), 7.18 (d, J = 7.6 Hz,1H), 7.13-7.06 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 147.8, 145.7, 137.6, 136.7, 135.3, 135.1, 133.9, 132.3, 131.1, 131.0, 129.6, 128.7, 128.5, 128.2, 128.1, 127.4, 127.3, 127.2, 127.1, 126.3, 121.4, 118.8; HRMS (ESI) calcd. for $C_{28}H_{18}BrN_2O$ ($M + H^+$), 477.0603; Found, 477.0582; IR (cm^{-1}) v 2930, 1711, 1600, 1542, 1482, 1466, 1288, 1134, 821, 758, 697.

9-fluoro-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3k**). White solid (yield 82%), mp: 223-224 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, J = 8.0 Hz, 1H), 7.74-7.69 (m, 2H), 7.67-7.59 (m, 3H), 7.54- 7.52 (m, 1H), 7.30-7.26 (m, 2H), 7.21 (d, J = 7.6 Hz, 1H), 7.11-7.06 (m, 6H), 7.03-7.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (d, $^1J_{CF}$ = 265 Hz), 158.3, 148.9, 148.4, 136.4, 135.3, 135.0, 134.5 (d, $^3J_{CF}$ = 10 Hz), 134.2, 132.4, 132.3, 131.1, 131.0, 128.9, 128.5 (d, $^4J_{CF}$ = 5 Hz), 128.1, 127.8, 127.4, 127.1 (d, $^4J_{CF}$ = 4 Hz), 126.8, 126.3, 122.6 (d, $^4J_{CF}$ = 4 Hz), 111.7 (d, $^2J_{CF}$ = 21 Hz), 110.0 (d, $^4J_{CF}$ = 7 Hz); HRMS (ESI) calcd. for $C_{28}H_{18}FN_2O$ ($M + H^+$) 417.1403; Found: 417.1413; IR (cm^{-1}) v 2933, 1710, 1611, 1544, 1488, 1444, 1284, 1141, 815, 777, 700.

3,11-dimethyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3l**). White solid (yield 80%), mp: 252-253 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 7.6 Hz, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.72-7.66 (m, 2H), 7.53 (s, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.28-7.24 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.12-7.02 (m, 6H),

6.95 (s, 1H), 2.55 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 147.8, 147.1, 145.4, 142.6, 137.3, 135.7, 135.3, 133.9, 132.3, 131.2, 131.0, 129.8, 128.9, 128.5, 128.0, 127.5, 127.2, 127.1, 126.8, 126.3, 126.1, 125.0, 117.8, 22.1, 22.0; HRMS (ESI) calcd. for $C_{30}H_{22}N_2NaO$ (M + Na^+), 449.1630; Found, 449.1652; IR (cm^{-1}) v 2918, 1729, 1610, 1543, 1487, 14639, 1287, 1124, 787, 695.

10-bromo-3-methyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3m**). White solid (yield 95%), mp: 254-255 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, J = 8.0 Hz, 1H), 8.23 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.28-7.21 (m, 3H), 7.12-7.05 (m, 7H), 6.93 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 147.9, 145.9, 143.0, 137.4, 136.9, 135.5, 135.3, 134.0, 131.1, 129.9, 129.5, 128.6, 128.5, 128.1, 128.0, 127.3, 127.2, 127.1, 126.9, 126.2, 124.8, 121.3, 118.4, 21.9; HRMS (ESI) calcd. for $C_{29}H_{20}BrN_2O$ (M + H^+), 491.0759; Found: 491.0740; IR (cm^{-1}) v 2923, 1689, 1597, 1541, 1489, 1463, 1292, 1153, 840, 728, 695.

3-chloro-11-methyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazo-lin-8-one (**3n**). White solid (yield 57%), mp: 286-287 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.56 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.20-7.15 (m, 4H), 7.05-6.96 (m, 8H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 147.0, 146.8, 145.7, 138.5, 136.8, 136.7, 135.3, 134.8, 131.1, 128.8, 128.7, 128.4, 128.2, 127.6, 127.5, 127.2, 127.1, 127.0, 126.4, 125.8, 125.6, 117.9, 22.1; HRMS (ESI) calcd. for $C_{29}H_{20}ClN_2O$ (M + H^+), 447.1264; Found: 447.1294; IR (cm^{-1}) v 2919, 1689, 1608, 1544, 1482, 1442, 1287, 1197, 875, 787, 708.

10-bromo-3-chloro-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3o**). white solid (yield 84%), mp: 232-233 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, J = 8.4 Hz, 1H), 8.23 (s, 1H), 7.82 (d, J = 7.2 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.30-7.24 (m, 3H), 7.17-7.04 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 147.1, 145.5, 138.9, 137.7, 136.5, 136.4, 135.3, 134.6, 131.0, 129.6, 128.9, 128.6, 128.4, 128.3, 127.7, 127.3, 127.3, 127.1, 125.7, 125.5, 121.4, 119.0; HRMS (ESI) calcd. for $C_{28}H_{17}BrClN_2O$ (M + H^+), 511.0213; Found: 511.0233; IR (cm^{-1}) v 2927, 1705, 1617, 1541, 1479, 1444, 1287, 1217, 885, 828, 696.

5,6-diethyl-3-methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3p**). White solid (yield 98%), mp: 103-104 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 7.6 Hz, 1H), 7.76-7.73 (m, 2H), 7.48 (s, 1H), 7.40 (t, J = 6.4 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 3.23 (q, J = 7.2 Hz, 2H), 2.91 (q, J = 7.2 Hz, 2H), 2.52 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 147.7, 146.8, 142.4, 137.5, 134.0, 132.7, 128.7, 127.5, 126.7, 126.4, 125.1, 125.0, 124.6, 123.0, 120.0, 23.5, 22.1, 20.5, 14.5, 14.2; HRMS (ESI) calcd. for $C_{21}H_{20}N_2NaO$ (M + Na^+) 339.1473; Found: 339.1493; IR (cm^{-1}) v 2964, 2873, 1684, 1603, 1541, 1468, 1296, 1180, 820, 764, 698.

3-methyl-5,6-dip-tolyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3q**). White solid (yield 93%), mp: 298-299 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 8.0Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 7.6 Hz, 2H), 6.96-6.93 (m, 7H), 2.36 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 147.8, 147.1, 142.6, 136.7, 136.2, 135.3, 134.3, 134.2, 132.6, 131.0, 129.6, 128.9, 128.7, 128.3, 128.0, 127.7, 127.2, 127.1, 126.6, 126.2, 125.2, 124.9, 120.2, 22.0, 21.4, 21.3; HRMS (ESI) calcd. for $C_{31}H_{24}N_2NaO$ (M + Na^+), 463.1786; Found, 463.1791; IR (cm^{-1}) v 2921, 1706, 1602, 1542, 1491, 1467, 1291, 1123, 831, 769, 694.

5,6-bis(4-methoxyphenyl)-3-methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3r**). White solid (yield 90%), mp: 276-278 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 7.2Hz, 1H), 7.42-7.35 (m, 2H), 6.99-6.95 (m, 5H), 6.82 (d, J = 8.4 Hz, 2H), 6.67 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.74 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 158.5, 158.0, 147.8, 147.1, 142.6, 135.4, 134.4, 134.3, 132.2, 129.7, 129.6, 129.6, 127.9, 127.5, 127.1, 127.1, 126.6, 126.1, 125.2, 124.9, 120.2, 113.5, 112.7, 55.2, 55.0, 22.0; HRMS (ESI) calcd. for $C_{31}H_{25}N_2O_3$ (M + H^+), 473.1865; Found, 473.1894; IR (cm^{-1}) v 2923, 1701, 1601, 1545, 1510, 1468, 1289, 1247, 1176, 830, 768, 694.

5,6-bis(4-fluorophenyl)-3-methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3s**). White solid (yield 90%), mp 249-250 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 7.6 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.81-7.77 (m, 2H), 7.43-7.36 (m, 2H), 7.05-6.95 (m, 6H), 6.85- 6.81 (m, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9 (d, $^1J_{CF}$ = 246 Hz), 161.4 (d, $^1J_{CF}$ = 245 Hz), 161.2, 147.4, 146.9, 142.9, 134.7, 134.5, 133.6, 133.1 (d, $^4J_{CF}$ = 4 Hz), 132.8 (d, $^3J_{CF}$ = 8.0 Hz), 131.4 (d, $^4J_{CF}$ = 3 Hz), 130.2 (d, $^3J_{CF}$ = 8.0 Hz), 130.1, 127.2, 127.1, 127.1,126.8, 125.9, 125.5, 124.9, 120.0, 115.3 (d, $^2J_{CF}$ = 21 Hz), 114.5 (d, $^2J_{CF}$ = 22 Hz), 22.0; HRMS (ESI) calcd. for $C_{29}H_{19}F_2N_2O$ (M + H^+), 449.1465; Found, 449.1488; IR (cm^{-1}) v 2921, 1681, 1600, 1548, 1508, 1467, 1293, 1223, 858, 778, 696.

5,6-bis(4-chlorophenyl)-3-methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**3t**). Light yellow solid (yield 88%), mp: 256-257 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 7.84-7.76 (m, 2H), 7.43 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 6.8 Hz, 1H), 7.28 (d, J = 7.6 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.98 (t, J = 9.6 Hz, 4H), 6.84 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 147.3, 146.9, 143.0, 135.5, 134.6, 133.8, 133.6, 133.3, 132.8, 132.4, 131.0, 130.2, 129.7, 128.9, 128.6, 127.7, 127.3, 127.1, 126.8, 125.9, 125.6, 125.0, 119.9, 22.0; HRMS (ESI), calcd. for $C_{29}H_{19}Cl_2N_2O$ (M + H^+), 481.0874; Found: 481.0883; IR (cm^{-1}) v 2927, 1708, 1602, 1542, 1489, 1467, 1291, 1095, 831, 768, 697.

2-methyl-5,6-diphenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**5a**). White solid (yield 49%), mp: 214-215 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 7.2 Hz, 1H), 7.73-7.71 (m, 1H), 7.54-7.52 (m, 1H), 7.40 (t, J = 8.0 Hz, 2H), 7.27-7.25 (m, 2H), 7.13-7.10 (m, 3H), 7.08-7.06 (m, 4H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 147.6, 146.9, 138.7, 137.1, 135.7, 134.4, 133.4, 132.3, 131.7, 131.1, 131.0, 128.9, 128.5, 128.0, 127.8, 127.2, 127.2, 126.9, 126.8, 126.7, 126.3, 125.6, 120.2, 21.7; HRMS (ESI) calcd. for $C_{29}H_{21}N_2O$ (M + H^+), 413.1654; Found, 413.1653; IR (cm^{-1}) v 2920, 1694, 1604, 1548, 1471, 1445, 1286, 1127, 770, 697.

5-(4-methoxyphenyl)-3-methyl-6-phenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**7a**). white solid, mp: 226-227 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.86-7.79 (m, 2H), 7.41 (t, J = 8.4 Hz, 2H), 7.31-7.24 (m, 3H), 7.10-7.04 (m, 2H), 6.97-6.95 (m, 3H), 6.65 (d, J = 8.0 Hz, 2H), 3.72 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 158.1, 147.8, 147.0, 142.7, 135.8, 135.1, 134.4, 134.0, 131.2, 129.7, 129.5, 128.1, 127.8, 127.1, 127.1, 126.7, 126.1, 125.3, 124.9, 120.2, 112.7, 55.0, 22.0; HRMS (ESI) calcd. for $C_{30}H_{23}N_2O_2$ (M + H^+), 443.1760; Found, 443.1736; IR (cm^{-1}) v 2930, 1699, 1605, 1545, 1492, 1467, 1293, 1246, 832, 779, 696.

6-(4-methoxyphenyl)-3-methyl-5-phenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (7b). White solid, mp: 272-273 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.44 (d, J

= 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.15-7.13 (m, 3H), 7.07-7.04 (m, 2H), 6.98 (d, *J* = 8.8 Hz, 3H), 6.81 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 158.5, 147.7, 147.0, 142.7, 137.3, 135.5, 134.4, 134.3, 132.2, 131.0, 129.8, 128.9, 128.5, 127.6, 127.2, 127.1, 126.8, 126.7, 126.2, 125.3, 124.9, 120.1, 113.5, 55.2, 22.0; HRMS (ESI) calcd. for $C_{30}H_{23}N_2O_2$ (M + H^+), 443.1760; Found, 443.1736; IR (cm^{-1}) v 2926, 1704, 1602, 1545, 1511, 1468, 1292, 1248, 828, 768, 694.

3,6-dimethyl-5-phenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**9a**). White solid, mp: 185-186 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 8.4 Hz, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.81 (m, 2H), 7.53 (t, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 6.8 Hz, 2H), 6.80 (s, 1H), 2.50 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 147.8, 147.1, 142.4, 137.2, 134.3, 134.2, 133.5, 130.7, 129.0, 128.9, 128.8, 128.0, 127.1, 126.9, 126.7, 125.5, 125.3, 124.6, 120.2, 21.9, 14.1; HRMS (ESI) calcd. for $C_{24}H_{19}N_2O$ (M + H^+), 351.1497; Found: 351.1492; IR (cm^{-1}) v 2917, 1701, 1606, 1537, 1491, 1466, 1296, 828, 774, 697.

3,5-dimethyl-6-phenyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (**9b**)**.** white solid, mp: 205-206 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.57 (s, 1H), 7.49-7.39 (m, 4H), 7.35 (t, J = 7.6 Hz, 1H), 7.31 (d, 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 147.4, 147.0, 142.6, 138.0, 134.3, 134.1, 133.8, 129.5, 128.6, 127.8, 127.4, 127.3, 127.1, 126.6, 125.1, 125.0, 123.9, 120.2, 119.9, 22.1, 15.1; HRMS (ESI) calcd. for $C_{24}H_{19}N_2O$ (M + H^+), 351.1497; Found, 351.1492; IR (cm^{-1}) v 2946, 1701, 1625, 1537, 1467, 1446, 1314, 828, 774, 642.

(*E*)-3-(1,2-diphenylvinyl)-2-propylquinazolin-4(3*H*)-one (**12**)**.** White solid, mp: 151-152 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (t, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 6.8 Hz, 3H), 7.37 (d, J = 8.0 Hz, 3H), 7.26 (t, J = 6.8 Hz, 3H), 7.23-7.18 (m, 3H), 6.84 (d, J = 7.2 Hz, 1H), 2.94 (t, J = 8.0 Hz, 2H), 1.94 (m, 2H), 1.05 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 166.1, 152.2, 150.4, 135.6, 134.0, 133.3, 132.6, 130.5, 129.4, 129.3, 129.2, 128.3, 127.9, 122.8, 119.5, 117.5, 111.6, 42.1, 22.4, 14.1; HRMS (ESI) calcd. for $C_{25}H_{19}N_2O$ (M + H^+), 351.1497; Found, 351.1492; IR (cm^{-1}) v 2927, 1642, 1580, 1466, 1349, 1214, 1137, 832, 774, 604.

Acknowlledgements

Financial support from National Natural Science Foudation of China (No. 21162012, 81261120413, and 21362014), Jiangxi Provincial Department of Science and Technoloy (for Jiangxi`s Key Laboratory of Green Chemistry, and no. 20122BAB203007), Jiangxi Educational Committee (GJJ10386), and Foundation for Young People (Yang Qin) of Jiangxi Normal University is gratefully acknowledged.

Notes and references

[a] *Key Laboratory of Small Fuctional Organic Molecule, Ministry of Education and College of Life Science, Jiangxi Normal University, Nanchang, Jiangxi 330022, China Fax: 0086-791-88120396; E-mail: yypeng@jxnu.edu.cn; yiyuanpeng@yahoo.com*

[b] *Jiangxi`s Key Laboratory of green chemistry and college of chemistry, Jiangxi Normal University, Nanchang, Jiangxi 330022, China*

† Electronic Supplementary Information (ESI) available: [characterization data: ^{1}H and ^{13}C NMR spectra of all compounds, X-ray data for compounds **3a**, **7b**, and **9b** (CIF)]. See DOI: 10.1039/b000000x/

1 Selected reviews: (*a*) J. A. Gladysz, *Chem. Rev.* 2011, **111**, No. 3 (2011 Frontiers in Transition Metal Catalyzed Reactions); (*b*) M. Beller and C. Bolm, *Transition metals for organic synthesis*; Wiley-VCH: New York, 2004; (*c*) A. de Meijere and F. Diederich, (eds); *Metal-catalyzed cross-coupling reactions*; Wiley-VCH: New York, 2004; (*d*) R. D. Larsen, *Organometallics in process chemistry*; Springer: Berlin, 2004.

2 T. Satoh and M. Miura, *Chem. Eur. J.* 2010, **16**, 11212.

3 (*a*) K. Ueura, T. Satoh and M. Miura, *Org. Lett.* 2007, **9**, 1407; (*b*) K. Ueura, T. Satoh and M. Miura, *J. Org. Chem.* 2007, **72**, 5362; (*c*) M. Shimizu, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.* 2009, **74,** 3478; (*d*) S. Mochida, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.* 2009, **74**, 6295.

4 (*a*) F. W. Patureau, T. Besset, N. Kuhl and F. Glorius, *J. Am. Chem. Soc.* 2011, **133**, 2154; (*b*) K. Muralirajan, K. Parthasarathy and C. Cheng, *Angew. Chem. Int. Ed.* 2011, **50**, 4169.

5 (*a*) T. Uto, M. Shimizu, K. Ueura, H. Tsurugi, T. Satoh and M. Miura, *J. Org. Chem.* 2008, **73**, 298; (*b*) M. Shimizu, H. Tsurugi, T. Satoh and M. Miura, *Chem. Asian J.* 2008, **3**, 881; (*c*) S. Mochida, M. Shimizu, K. Hirano, T. Satoh and M. Miura, *Chem. Asian J.* 2010, **5**, 847.

6 (*a*) S. Lim, J. H. Lee, C. W. Moon, J. Hong and C. Jun, *Org. Lett.* 2003, **5**, 2759; (*b*) D. A. Colby, R. G. Bergman and J. A. Ellman, *J. Am. Chem. Soc.* 2006, **128**, 5604; (*c*) D. A. Colby, R. G. Bergman and J. A. Ellman, *J. Am. Chem. Soc.* 2008, **130**, 3645; (*d*) L. Li, W. W. Brennessel and W. D. Jones, *J. Am. Chem. Soc.* 2008, **130**, 12414; (*e*) T. Fukutani, N. Umeda, K. Hirano, T. Satoh and M. Miura, *Chem. Commun.* 2009, 5141; (*f*) N.Guimond and K. Fagnou, *J. Am. Chem. Soc.* 2009, **131**, 12050.

7 (a) K. Parthasarathy and C. Cheng, *J. Org. Chem.* 2009, **74**, 9359; (*b*) X. Zhang, D. Chen, M. Zhao, J. Zhao, A. Jia and X. Li, *Adv. Synth. Catal.* 2011, **353**, 719.

8 (*a*) T. K. Hyster and T. Rovis, *J. Am. Chem. Soc.* 2010, **132**, 10565; (*b*) R. Álvarez, C. Martínez, Y. Madich, J. G. Denis, J. M. Aurrecoechea and A. R. Lera, *Chem. Eur. J.* 2010, **16,** 12746; (*c*) N. Zhang, B. Li, H. Zhong and J. Huang, *Org. Biomol. Chem.* 2012, **10**, 9429; (*d*) Y. Kajita, S. Matsubara and T. Kurahashi, *J. Am. Chem. Soc.* 2008, **130**, 6058; (*e*)H. Shiota, Y. Ano, Y. Aihara, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.* 2011, **133**, 14952.

9 (*a*) N. Guimond, C. Gouliaras and K. Fagnou, *J. Am. Chem. Soc.* 2010, **132**, 6908; (*b*) N. Guimond, S. I. Gorelsky and K. Fagnou, *J. Am. Chem. Soc.* 2011, **133**, 6449.

10 (a) P. C. Too, Y. Wang and S. Chiba, *Org. Lett.* 2010, **12**, 5688; (*b*) P. C. Too, S. H. Chua, S. H. Wong and S. Chiba, *J. Org. Chem.* 2011, **76**, 6159.

11 (*a*) J. Chen, G. Song, C. Pan and X. Li, *Org. Lett.* 2010, **12**, 5426; (*b*) J. Barluenga, M. Fañanás-Mastral, F. Aznar and C. Valdés, *Angew. Chem. Int. Ed.* 2008, **47**, 6594.

12 (a) D. R. Stuart, M. Bertrand-Laperle,K. M. N. Burgess and K. Fagnou, *J. Am. Chem. Soc.* 2008, **130**, 16474; (*b*) D. R. Stuart, P. Alsabeh, M; Kuhn and K. Fagnou, *J. Am. Chem. Soc.* 2010, **132**, 18326.

13 (a) Y. Su, M. Zhao, K. Han, G. Song and X. Li, *Org. Lett.* 2010, **12**, 5462; (*b*) T. K. Hyster and T. Rovis, *Chem. Sci.* 2011, **2**, 1606.

14 S. Rakshit, F. W. Patureau and F. Glorius, *J. Am. Chem. Soc.* 2010, **132**, 9585.

15 M. P. Huestis, L. Chan, D. R. Stuart and K. Fagnou, *Angew. Chem. Int. Ed.* 2011, **50**, 1338.

16 (*a*) Y. Wang, K. K. Toh, J. Lee and S. Chiba, *Angew. Chem. Int. Ed.* 2011, **50**, 5927; (*b*) T. Miura, M. Yamauchi and M. Murakami, *Org. Lett.* 2008, **10**, 3085.

17 (*a*) N. Umeda, H. Tsurugi, T. Satoh and M. Miura, *Angew. Chem. Int. Ed.* 2008, **47**, 4019; (*b*) K. Morimoto, K. Hirano, T. Satoh and M. Miura, *Org. Lett.* 2010, **12**, 2068; (*c*) G. Zhang, L. Yang, Y. Wang, Y. Xie and H. Huang, *J. Am. Chem. Soc.* 2013, **135**, 8850.

18 (*a*) L. Ackermann, A. V. Lygin and N. Hofmann, *Org. Lett.* 2011, **13**, 3278; (*b*) L. Ackermann and S. Fenner, *Org. Lett.* 2011, **13**, 6548; (*c*) L. Ackermann, A. V. Lygin, N. Hofmann, *Angew. Chem. Int. Ed.* 2011, **50**, 6379; (*d*) B. Li, H. Feng, S. Xu and B. Wang, *Chem. Eur. J.* 2011, **17**, 12573; (*e*) L. Ackermann, L. Wang and A. V. Lygin, *Chem. Sci.* 2012, **3**, 177; (*f*) L. Ackermann and A. V. Lygin, *Org. Lett.* 2012, **14**, 764; (*g*) M. Deponti, S. I. Kozhushkov, D. S. Yufit and L. Ackermann, *Org. Biomol. Chem.* 2013, **11**, 142; (*h*) L. Wang and L. Ackermann, *Org. Lett.* 2013, **15**, 176; (*i*) P. Villuendas and E. P. Urriolabeitia, *J. Org. Chem.* 2013, **78**, 5254; (*j*) W. Ma, K. Graczyk and L. Ackermann, *Org. Lett.* 2012, **14**, 6318; (*k*) C. Kornhaaß, J. Li and L. Ackermann, *J. Org. Chem.* 2012, **77**, 9190.

19 (a) T. Eicher and S. Hauptmann, *The Chemistry of Heterocycles*; Wiley-VCH: Weinheim, 2003; (*b*) A. R. Katrizky and A. F. Pozharskii, *Handbook of Heterocyclic Chemistry*, 2nd ed.; Pergamon: Amsterdam, 2000; (*c*) M. H. Elnagdi, S. A. S. Ghozlan

and I. A. Abdelhamid, *Arkivoc* 2008, 54; (*d*) S. K. Meegalla, G. J. Stevens, C. A. McQueen, A. Y. Chen, C. Yu, L. F. Liu, L. R. Barrows and E. J. LaVoie, *J. Med. Chem.* 1994, **37**, 3434; *(e)* Y. H. Hong, W. J. Lee, S. H. Lee, J. K. Son, H. Kim, J. M. Nam, Y. Kwon and Y. Jahng, *Biol. Pharm. Bull.* 2010, **33**, 1704.

20 (*a*) G. Song, D. Chen,C. Pan, R. H. Crabtree and X. Li, *J. Org. Chem.* 2010, **75**, 7487; (*b*) B. Li, H. Feng, N. Wang, J. Ma, H. Song, S. Xu and B.Wang, *Chem. Eur. J.* 2012, **18**, 12873.

21 Y. Y. Peng, G. Y. S. Qiu, Q. Yang, J. J. Yuan and Z. H. Deng, Z. H. *Synthesis* 2012, **44**, 1237.

View Article Online
DOI: 10.1039/C3OB41955J