Synthesis W.-C. Pan et al. Paper

Silver Triflate Catalyzed Synthesis of Isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazoline Derivatives via Alkyne Hydroamination

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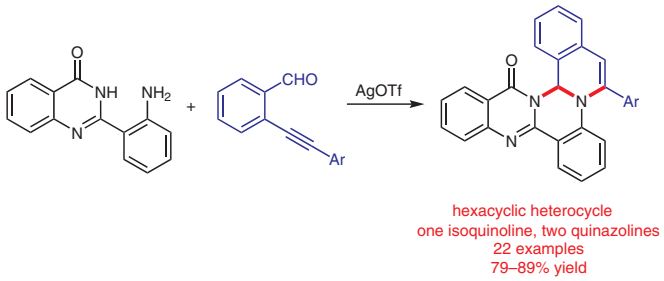

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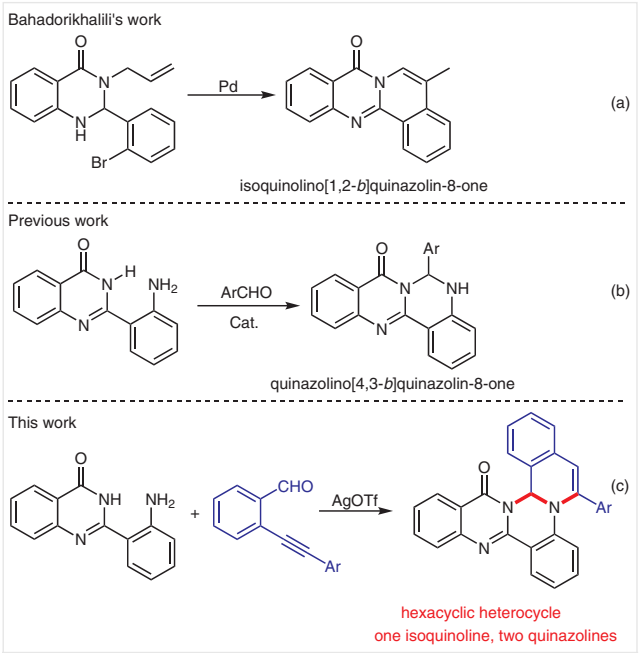
Abstract Using 2-(2-aminophenyl)quinazolin-4(3*H*)-one and 2-(2-phenylethynyl)benzaldehyde as the reactants, silver triflate (AgOTf) was proved to be an efficient catalyst to promote not only quinazoline cyclization, but also the intramolecular hydroamination of alkyne for the synthesis of 6-aryl-17*H*,18a*H*-isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17-one derivatives in high yields.

Key words isoquinoline, quinazoline, hydroamination, AgOTf, synthesis

Isoquinoline and quinazoline are both bicyclic nitrogenous heterocycles and medicinal molecular skeleton.[1] They both possess a benzene ring and a six-membered heterocycle but bearing different numbers of nitrogen atoms. Along with the difference in their structures, it was reported that they also indicated various kinds of bioactivities. As we all know, the isoquinoline moieties are well known for their anti-inflammatory activities,[2] while quinazolines are famous for their antitumor activities.[3] Some of them have been developed as the clinical drugs, for example, atracurium besylate[4] and vandetanib.[5]

According to the development of medicinal chemistry, more and more attention has been devoted to the combination of two different types of heterocycles. The aim is to obtain structurally diversified heterocycles to further enhance the medicinal effect, or gain novel anti-inflammatory or antitumor activity via bioscreening. In view of the importance of isoquinoline and quinazoline, lots of novel procedures have been established for the construction of isoquinolinoquinazolines[6] and quinazolinoquinazolines[7] in recent years. In 2018, Bahadorikhalili[8] group reported a palladium-catalyzed intramolecular Heck reaction of 3-allyl-2-(2-bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-ones (Scheme 1a). It was an efficient isoquinoline construction based on quinazoline moiety. However, a costly Pd was used as the catalyst. In our previous paper, cyclization of 2-(*o*-aminophenyl)-4(3*H*)-quinazolinone with aromatic aldehydes was developed as a very rapid method to build quinazolinoquinazoline derivatives (Scheme 1b).[9]



Scheme 1 Approach to heterocycles containing isoquinoline and quinazoline

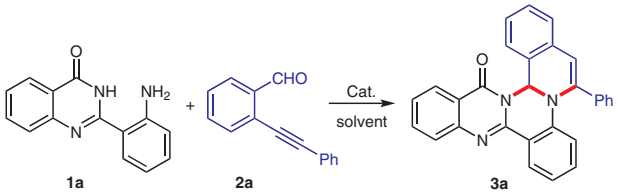
To the best of our knowledge, there is no study concerning about the synthesis of isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolines, and it is a novel fused hexacyclic moiety bearing both isoquinoline and two quinazolines. In our investigation, hydroamination of alkyne is an efficient method to build nitrogenous six-membered ring especially for isoquinoline analogue.[10] Therefore, we reasoned that the

first condensation cyclization, and then hydroamination cyclization would take place (Scheme 1c) when 2-(*o*-aminophenyl)quinazolin-4(3*H*)-one (**1a**) was submitted to react with 2-(2-phenylethynyl)benzaldehyde (**2a**). Taking this good idea, we performed the designed reaction in our lab catalyzed by silver triflate (AgOTf),[11] which is a powerful reagent to activate the C≡C bond. To our delight, the desired twice cascade cyclizations occurred to give 6-phenyl-17*H*,18a*H*-isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17-one (**3a**) in high yield (Table 1). As our ongoing study toward polycyclic heterocycles,[12] herein, we would like to report the synthesis of fused hexacyclic isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolines catalyzed by AgOTf.

As depicted in Table 1, we began our study to optimize the reaction conditions using the reaction of **1a** and **2a** as a model. The first screening was to change various kinds of catalysts. The Lewis acids, such as CuI, CuBr, $Cu(OTf)_2$, $Yb(OTf)_3$, $Sc(OTf)_3$, $Zn(OTf)_2$, $Bi(OTf)_3$, AgOAc, and AgOTf were all tested in this reaction. Ag(I) indicated the best catalytic effect, and the next was Yb(III) in the metal cations. The best anion was TfO^- for this conversion, and 5 mol% AgOTf gave an obviously higher yield (83%). $Zn(OTf)_2$, Cu(I), and Cu(II) almost had no catalytic activity for this cascade reaction. Furthermore, 5 mol% AgOTf was enough to promote the twice cyclizations, and the reaction gave the same yield when 10 mol% AgOTf was used. However, the yield decreased obviously using 1 mol% amount of AgOTf. In the following solvent screening, it was found that it had a slight effect on the yields. To our delight, the reaction yield could be improved to 86% when DMSO was used as a solvent. Furthermore, the aprotic polar solvents, such as DMF, DMA, and DMSO were in favor of the reaction, while toluene and 1,4-dioxane led to slightly lower yields.

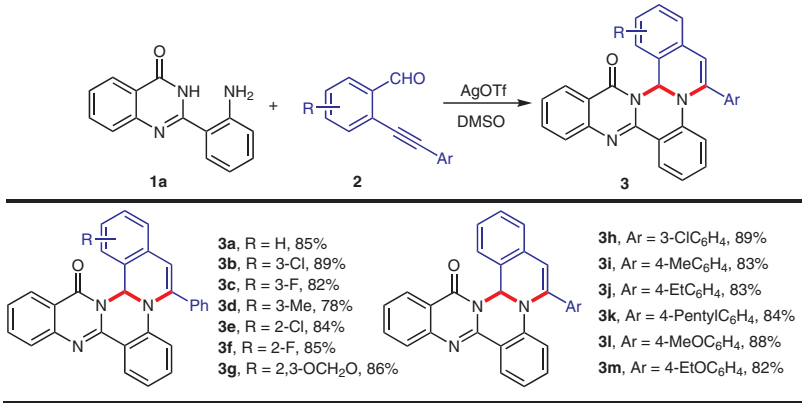
Through above screening, we obtained the optimal reaction condition that was catalyzed by 5 mol% AgOTf in DMSO at 100 °C. The next step was to test the adaptability of the two substances. In our lab, the 2-(*o*-aminophenyl)-4(3*H*)-quinazolinone (**1a**) was used as an unchanged reactant first, and varied the different substituents on the 2-(2-arylethynyl)benzaldehydes **2** to react with **1a** one by one under the optimal reaction conditions. Compound **2** bearing two benzene rings whether carrying electron-donating substituent (methyl, methoxy, ethyl, pentyl, and ethoxy) or electron-drawing group (fluoro and chloro), all underwent the condensation and hydroamination to give **3a–m** in good to high yields (Scheme 2).

Table 1 Optimization of the Reaction Conditions[a]



Entry	Catalyst (mol%)	Solvent	Yield (%)[b]
1	CuI (5)	DMF	trace
2	CuBr (5)	DMF	trace
3	$Cu(OTf)_2$ (5)	DMF	trace
4	$Yb(OTf)_3$ (5)	DMF	72
5	$Sc(OTf)_3$ (5)	DMF	69
6	$Zn(OTf)_2$ (5)	DMF	trace
7	$Bi(OTf)_3$ (5)	DMF	32
8	AgOAc (5)	DMF	59
9	AgOTf (5)	DMF	83
10	AgOTf (10)	DMF	83
11	AgOTf (1)	DMF	52
12	AgOTf (5)	DME	69
13	AgOTf (5)	DMSO	85
14	AgOTf (5)	DMA	83
15	AgOTf (5)	1,4-dioxane	78
16	AgOTf (5)	toluene	72

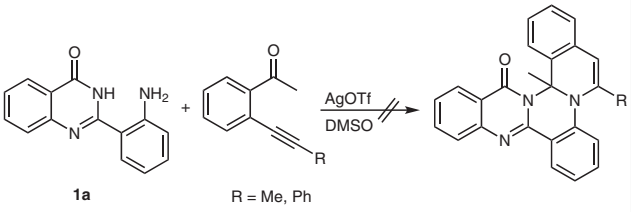
[a] Reaction conditions: **1a** (118 mg, 0.5 mmol), **2a** (113 mg, 0.55 mmol), solvent (5.0 mL), 100 °C, 10 h.
[b] Isolated yield.



Scheme 2 The cascade reaction with various ethynylbenzaldehydes. *Reagents and conditions*: **1a** (118 mg, 0.5 mmol), **2** (0.55 mmol), AgOTf (6 mg, 0.025 mmol), DMSO (5.0 mL), 100 °C. Isolated yields are shown.

However, when 1-[2-(phenylethynyl)phenyl]ethan-1-one or 1-[2-(prop-1-yn-1-yl)phenyl]ethan-1-one was used as a reactant to react with **1a** under the optimal reaction conditions (Scheme 3), no reaction was observed by TLC. Perhaps, the activity of ketone is lower than that of aldehyde.

The structure of **3l** was unambiguously confirmed by X-ray diffraction analysis, and its crystal structure is shown in Figure 1. X-ray diffraction analysis of **3l** indicates that the newly formed quinazoline moiety is slightly distorted, and the pyrimidine adopts a skew boat confirmation. The atoms N3 and C22 deviate the defined plane (N1, C8–C14) by 0.271(2) and 0.679(2) Å, respectively. The isoquinoline is also a twisted moiety while the pyridine ring adopts a skew confirmation. The atoms C1–C6 and C22–C23 are coplanar with mean deviation being 0.029(2) Å while C7 and C8 deviate from the basal plane by 0.423(2) and 0.817(2) Å, respectively. Another quinazoline ring is a plane moiety. X-ray diffraction analysis also reveals that the newly formed quinazoline ring is nearly parallel to another quinazoline forming a dihedral angle of 10.6 (1)°, and it is nearly perpendicular to isoquinoline ring forming a dihedral angle of 89.8 (1)°. In addition, the isoquinoline ring makes a dihedral angle of 22.9 (1)° to its connected benzene ring (C24–C29).



Scheme 3 Attempts at reactions involving ketones

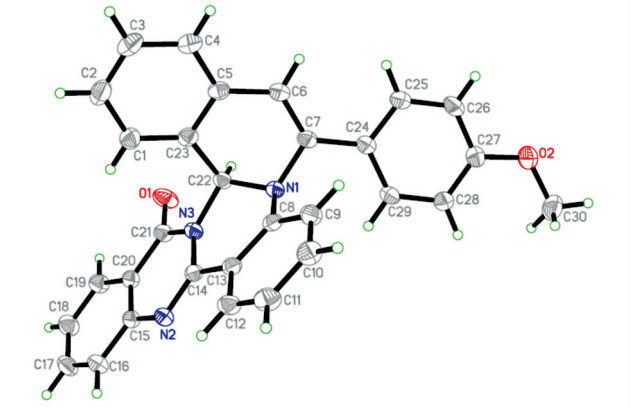


Figure 1 The crystal structure of **3l** shown in 30% probability

After careful examination of the reactant **2**, we next turned to prepare several 2-(2-aminophenyl)quinazolin-4(3*H*)-ones **1** via a two-step reaction. The first is a condensation cyclization of 2-aminobenzamides with 2-nitrobenzaldehyde followed by a reductive reaction of nitro group using 85% hydrazine hydrate as a reductant in the presence of $FeCl_3$. Subsequently, **1** was submitted to react with **2** at 100 °C in DMSO using 5 mol% AgOTf as a catalyst, and afforded **3n–v** in 79–87% yields as expected. The substituents on two benzene rings also had no obvious influence on the reaction yields (Scheme 4).

In conclusion, an efficient method for the synthesis of 6-aryl-17*H*,18a*H*-isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17-ones has been established via a reaction of 2-(2-aminophenyl)quinazolin-4(3*H*)-ones and 2-(2-arylethynyl)benzaldehydes. AgOTf proved to be an efficient catalyst to activate the C=N and C≡C bonds, which undergo two cyclization leading to hexacyclic heterocycles containing both isoquinoline and two quinazoline moieties.

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrophotometer in KBr pellets. ^{1}H NMR spectra were obtained from a solution in $CDCl_3$ with Me_4Si as internal standard using a Bruker 400 spectrometer. HRMS analyses were carried out using a Bruker micro-TOF-Q-MS analyzer. All the chemicals were obtained from Beijing InnoChem Science & Technology Co., Ltd except for DMF and EtOH, which were purchased from Sinopharm Chemical Reagent Co., Ltd.

6-Phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3a); Typical Procedure

2-(2-Aminophenyl)quinazolin-4(3*H*)-one (**1a**; 118 mg, 0.5 mmol), 2-(phenylethynyl)benzaldehyde (**2a**; 113 mg, 0.55 mmol), and AgOTf (6 mg, 0.025 mmol) were added to a dry reaction flask with high vacuum valve. After three times in vacuum and replacement of N_2, DMSO (5.0 mL) was injected into the mixture. Before reaching completion, the reaction mixture was stirred and heated at 100 °C under N_2 atmosphere. The mixture was poured into H_2O (50 mL), and the yellow precipitate formed was collected by filtration. The crude product was purified by chromatography over silica gel using EtOAc and petroleum ether (1:5) as an eluent to give **3a**; yield: 181 mg (85%); pale yellow solid; mp 267–268 °C.

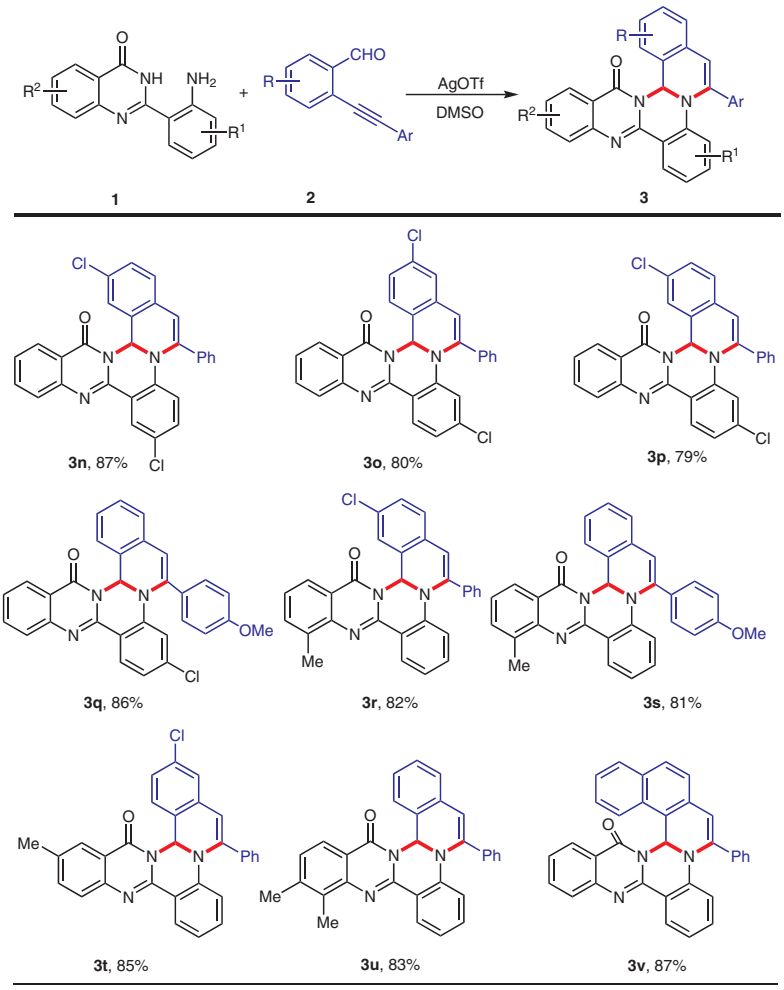
The products **3** were obtained with residual solvents, such as EtOAc or petroleum ether as observed by NMR spectroscopy, and were hard to be removed (see Supporting Information).

IR (KBr): 3063, 1652, 1610, 1574, 1509, 1488, 1473, 1454, 1391, 1345, 1332, 1293, 1243, 1196, 1175, 1158, 1129, 1051, 949, 903, 891, 771, 747, 693 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.35 (d, *J* = 8.8 Hz, 1 H, CH), 6.73 (d, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 7.01–7.05 (m, 1 H, ArH), 7.14 (t, *J* = 7.6 Hz, 1 H, ArH), 7.23–7.31 (m, 4 H, ArH), 7.37–7.45 (m, 3 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.83–7.87 (m, 4 H, ArH), 8.35 (dd, *J* = 8.0 Hz, *J′* = 1.2 Hz, 1 H, ArH), 8.39 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.7, 117.2, 117.8, 118.3, 120.3, 121.1, 120.3, 125.9, 126.1, 126.6, 127.3, 127.4, 127.8, 128.4, 128.6, 129.2, 129.4, 130.4, 132.8, 133.0, 134.89, 134.93, 142.9, 143.1, 146.9, 148.4, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{30}N_3O$ [M + H]$^+$: 426.1601; found: 426.1606.



Scheme 4 Structurally diversified products **3**. *Reagents and conditions*: **1** (0.5 mmol), **2** (0.55 mmol), AgOTf (6 mg, 0.025 mmol), DMSO (5.0 mL), 100 °C. Isolated yields are shown.

3-Chloro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3b)

Yield: 205 mg (89%); pale yellow solid; mp 269–270 °C.

IR (KBr): 3056, 1683, 1611, 1587, 1561, 1487, 1474, 1465, 1448, 1392, 1342, 1329, 1315, 1277, 1247, 1155, 1133, 1085, 1024, 932, 895, 877, 764 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.33 (d, *J* = 8.0 Hz, 1 H, CH), 6.66 (d, *J* = 8.0 Hz, 1 H, ArH), 6.89–6.93 (m, 1 H, ArH), 7.04–7.12 (m, 2 H, ArH), 7.17 (s, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.30 (d, *J* = 2.0 Hz, 1 H, ArH), 7.41–7.47 (m, 3 H, ArH), 7.51–7.55 (m, 1 H, ArH), 7.82–7.87 (m, 4 H, ArH), 8.34 (dd, *J* = 7.6 Hz, *J′* = 1.2 Hz, 1 H, ArH), 8.38 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.4, 116.6, 117.2, 118.3, 120.2, 121.4, 124.5, 125.9, 126.1, 126.8, 127.3, 127.5, 127.8, 128.1, 128.7, 129.3, 129.8, 133.1, 134.4, 134.45, 134.48, 135.1, 142.6, 144.4, 146.6, 148.3, 160.7.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{19}ClN_3O$ [M + H]$^+$: 460.1211; found: 460.1208.

3-Fluoro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3c)

Yield: 182 mg (82%); pale yellow solid; mp 229–230 °C.

IR (KBr): 3061, 1652, 1610, 1559, 1589, 1571, 1474, 1463, 1448, 1392, 1330, 1316, 1234, 1156, 1145, 1127, 1099, 1024, 958, 892, 761 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.34 (d, *J* = 8.4 Hz, 1 H, CH), 6.67–6.70 (m, 1 H, ArH), 6.79–6.84 (m, 1 H, ArH), 6.90 (t, *J* = 7.6 Hz, 1 H, ArH), 7.00–7.07 (m, 2 H, ArH), 7.19 (s, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.38–7.46 (m, 3 H, ArH), 7.50–7.54 (m, 1 H, ArH), 7.82–7.87 (m, 4 H, ArH), 8.35 (dd, *J* = 8.0 Hz, *J′* = 1.2 Hz, 1 H, ArH), 8.80 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.4, 113.0 (d, $J_{C,F}$ = 22.9 Hz), 114.8 (d, $J_{C,F}$ = 22.1 Hz), 116.9 (d, $J_{C,F}$ = 2.3 Hz), 117.2, 118.4, 120.2, 121.3, 124.8 (d, $J_{C,F}$ = 8.8 Hz), 126.1, 126.7, 127.3, 127.5, 127.8, 129.3, 129.8, 133.0, 134.5, 134.7 (d, $J_{C,F}$ = 8.8 Hz), 135.0, 142.7, 144.3, 146.7, 148.3, 160.7, 162.9 (d, $J_{C,F}$ = 244.6 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz): δ = 113.507.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{19}FN_3O$ [M + H]$^+$: 444.1507; found: 444.1506.

3-Methyl-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3d)

Yield: 171 mg (78%); pale yellow solid; mp 271–272 °C.

IR (KBr): 3080, 3065, 3034, 1679, 1610, 1587, 1471, 1392, 1341, 1292, 1241, 1181, 1154, 1134, 1049, 1023, 911, 869, 766 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.27 (s, 3 H, CH_3), 6.35 (d, *J* = 8.4 Hz, 1 H, CH), 6.61 (d, *J* = 7.6 Hz, 1 H, ArH), 6.86 (t, *J* = 7.6 Hz, 1 H, ArH), 6.93 (d, *J* = 7.6 Hz, 1 H, ArH), 7.00–7.05 (m, 1 H, ArH), 7.10 (s, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.23 (s, 1 H, ArH), 7.35–7.44 (m, 3 H, ArH), 7.48–7.52 (m, 1 H, ArH), 7.80–7.86 (m, 4 H, ArH), 8.34 (dd, *J* = 7.6 Hz, *J′* = 0.8 Hz, 1 H, ArH), 8.38 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.2, 66.7, 117.2, 118.0, 118.3, 120.3, 121.0, 123.0, 125.8, 126.6, 126.9, 127.3, 127.4, 127.7, 127.8, 129.1, 129.2, 129.3, 132.7, 133.0, 134.9, 135.0, 138.3, 142.9, 143.3, 147.0, 148.4, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{22}N_3O$ $[M + H]^+$: 440.1757; found: 440.1756.

2-Chloro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3e)

Yield: 193 mg (84%); pale yellow solid; mp 248–249 °C.

IR (KBr): 3065, 2916, 1675, 1620, 1605, 1560, 1492, 1482, 1473, 1463, 1388, 1324, 1251, 1210, 1133, 1050, 904, 871, 833, 763, 747 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.34 (dd, *J* = 8.0 Hz, *J′* = 0.4 Hz, 1 H, CH), 6.69 (s, 1 H, ArH), 6.90–6.94 (m, 1 H, ArH), 7.04–7.08 (m, 1 H, ArH), 7.18 (d, *J* = 0.8 Hz, 1 H, ArH), 7.23–7.24 (m, 3 H, ArH), 7.40–7.45 (m, 3 H, ArH), 7.52–7.56 (m, 1 H, ArH), 7.81–7.87 (m, 4 H, ArH), 8.36 (dd, *J* = 7.6 Hz, *J′* = 1.2 Hz, 1 H, ArH), 8.38–8.40 (m, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.3, 116.8, 117.2, 118.4, 120.2, 121.4, 123.5, 125.9, 126.8, 127.2, 127.4, 127.5, 127.9, 128.9, 129.2, 129.6, 131.4, 132.1, 133.0, 134.3, 134.5, 135.1, 142.7, 143.3, 146.6, 148.3, 160.7.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{19}ClN_3O$ $[M + H]^+$: 460.1211; found: 460.1203.

2-Fluoro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3f)

Yield: 188 mg (85%); pale yellow solid; mp 272–273 °C.

IR (KBr): 3064, 3038, 2950, 1679, 1610, 1586, 1559, 1507, 1492, 1483, 1396, 1330, 1316, 1267, 1245, 1186, 1150, 1049, 1024, 947, 899, 846, 829, 775, 744 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.36 (d, *J* = 8.0 Hz, 1 H, CH), 6.46 (dd, *J* = 8.0 Hz, *J′* = 1.6 Hz, 1 H, ArH), 6.89–6.97 (m, 2 H, ArH), 7.04–7.08 (m, 1 H, ArH), 7.19 (s, 1 H, ArH), 7.24–7.29 (m, 2 H, ArH), 7.36–7.44 (m, 3 H, ArH), 7.51–7.55 (m, 1 H, ArH), 7.81–7.88 (m, 4 H, ArH), 8.35–8.40 (m, 2 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.3, 111.1 (d, $J_{C,F}$ = 23.4 Hz), 115.6 (d, $J_{C,F}$ = 21.9 Hz), 116.8, 117.1, 118.3, 120.2, 121.3, 125.8, 126.8, 127.3, 127.5, 127.7 (d, $J_{C,F}$ = 8.1 Hz), 127.9, 129.0 (d, $J_{C,F}$ = 3.3 Hz), 129.2, 129.4, 132.9 (d, $J_{C,F}$ = 6.5 Hz), 133.0, 134.7, 135.1, 142.4 (d, $J_{C,F}$ = 2.4 Hz), 142.9, 146.6, 148.3, 160.7, 163.0 (d, $J_{C,F}$ = 248.6 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz): δ = 111.546.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{19}FN_3O$ $[M + H]^+$: 444.1507; found: 444.1500.

11-Phenyl-[1,3]dioxolo[4′,5′:6,7]isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-19(17b*H*)-one (3g)

Yield: 202 mg (86%); pale yellow solid; mp 280–281 °C.

IR (KBr): 3062, 2924, 2852, 1679, 1609, 1588, 1576, 1494, 1472, 1464, 1447, 1431, 1394, 1319, 1290, 1262, 1112, 1032, 965, 829 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 5.86 (s, 2 H, OCH_2O), 6.22 (s, 1 H, ArH), 6.36 (d, *J* = 8.4 Hz, 1 H, CH), 6.78 (s, 1 H, ArH), 6.89–6.93 (m, 1 H, ArH), 7.05–7.09 (m, 1 H, ArH), 7.15 (d, *J* = 0.8 Hz, 1 H, ArH), 7.16 (s, 1 H, ArH), 7.35–7.44 (m, 3 H, ArH), 7.50–7.54 (m, 1 H, ArH), 7.79–7.85 (m, 4 H, ArH), 8.35 (dd, *J* = 8.0 Hz, *J′* = 1.6 Hz, 1 H, ArH), 8.37–8.39 (m, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.4, 101.4, 104.6, 106.7, 117.1, 117.6, 118.4, 120.2, 121.1, 124.8, 125.7, 126.6, 127.1, 127.3, 127.4, 127.8, 129.09, 129.13, 133.0, 134.8, 135.0, 141.4, 143.2, 146.8, 147.8, 148.1, 148.3, 160.7.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{20}N_3O_3$ $[M + H]^+$: 470.1499; found: 470.1475.

6-(3-Chlorophenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3h)

Yield: 205 mg (89%); pale yellow solid; mp 273–274 °C.

IR (KBr): 3068, 3058, 2923, 1675, 1608, 1588, 1575, 1558, 1473, 1459, 1416, 1386, 1341, 1277, 1235, 1200, 1128, 1077, 1052, 907, 881, 790, 760 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.32 (d, *J* = 8.4 Hz, 1 H, CH), 6.73 (d, *J* = 7.6 Hz, 1 H, ArH), 6.90 (t, *J* = 7.6 Hz, 1 H, ArH), 7.07 (t, *J* = 7.6 Hz, 1 H, ArH), 7.16 (t, *J* = 7.6 Hz, 1 H, ArH), 7.21 (s, 1 H, ArH), 7.24–7.31 (m, 3 H, ArH), 7.35 (s, 1 H, ArH), 7.36 (s, 1 H, ArH), 7.50–7.54 (m, 1 H, ArH), 7.71–7.73 (m, 1 H, ArH), 7.83–7.87 (m, 3 H, ArH), 8.36 (d, *J* = 8.0 Hz, 1 H, ArH), 8.39 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.6, 117.0, 118.4, 119.1, 120.3, 121.3, 123.1, 124.0, 125.8, 126.3, 126.7, 127.3, 127.5, 127.8, 128.7, 128.9, 129.3, 130.46, 130.49, 132.4, 133.0, 135.0, 135.3, 136.9, 141.6, 142.8, 146.8, 148.3, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{19}ClN_3O$ $[M + H]^+$: 460.1211; found: 460.1211.

6-(*p*-Tolyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3i)

Yield: 182 mg (83%); pale yellow solid; mp 260–261 °C.

IR (KBr): 3059, 3024, 2920, 1672, 1611, 1588, 1559, 1509, 1473, 1394, 1335, 1317, 1295, 1203, 1183, 1155, 1131, 1050, 1018, 1007, 965, 859, 797, 742 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.39 (s, 3 H, CH_3), 6.36 (d, *J* = 8.4 Hz, 1 H, CH), 6.72 (d, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 7.01–7.05 (m, 1 H, ArH), 7.12 (t, *J* = 7.6 Hz, 1 H, ArH), 7.21–7.29 (m, 6 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.72 (s, 1 H, ArH), 7.74 (s, 1 H, ArH), 7.81–7.87 (m, 2 H, ArH), 8.34 (dd, *J* = 8.0 Hz, *J′* = 1.2 Hz, 1 H, ArH), 8.38 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.4, 66.7, 116.9, 117.2, 118.3, 120.3, 121.0, 123.0, 125.8, 125.9, 126.6, 127.3, 127.4, 127.8, 128.2, 128.5, 129.9, 130.3, 132.1, 132.9, 133.0, 134.9, 139.6, 143.0, 143.2, 147.0, 148.4, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{22}N_3O$ $[M + H]^+$: 440.1757; found: 440.1751.

6-(4-Ethylphenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3j)

Yield: 188 mg (83%); pale yellow solid; mp 289–290 °C.

IR (KBr): 2970, 2958, 2926, 1672, 1589, 1571, 1473, 1460, 1390, 1342, 1330, 1238, 1144, 1061, 1007, 972, 904, 891, 838, 762 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.27 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.70 (q, *J* = 7.6 Hz, 2 H, CH_2), 6.37 (d, *J* = 8.0 Hz, 1 H, CH), 6.72 (d, *J* = 7.2 Hz, 1 H, ArH), 6.88 (t, *J* = 7.6 Hz, 1 H, ArH), 7.05 (t, *J* = 8.0 Hz, 1 H, ArH), 7.13 (t, *J* = 7.2 Hz, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.23 (s, 1 H, ArH), 7.26–7.30 (m, 4 H, ArH), 7.50–7.54 (m, 1 H, ArH), 7.75 (d, *J* = 8.0 Hz, 2 H, ArH), 7.82–7.87 (m, 2 H, ArH), 8.34 (d, *J* = 8.0 Hz, 1 H, ArH), 8.39 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.3, 28.7, 66.7, 117.0, 117.3, 118.3, 120.3, 120.9, 123.0, 125.9, 126.0, 126.5, 127.3, 127.8, 128.2, 128.5, 128.7, 130.3, 132.3, 132.9, 133.0, 134.9, 143.0, 143.2, 145.8, 147.0, 148.4, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{31}H_{24}N_3O$ $[M + H]^+$: 454.1914; found: 454.1915.

6-(4-Pentylphenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3k)

Yield: 208 mg (84%); pale yellow solid; mp 214–215 °C.

IR (KBr): 3067, 2922, 2851, 1684, 1606, 1589, 1560, 1509, 1474, 1465, 1395, 1329, 1293, 1249, 1175, 1156, 1026, 832, 762, 695 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 0.90 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.32–1.37 (m, 4 H, 2 × CH_2), 1.63–1.68 (m, 2 H, CH_2), 2.63 (t, *J* = 7.6 Hz, 2 H, CH_2), 6.37 (d, *J* = 8.0 Hz, 1 H, CH), 6.72 (d, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 7.02–7.06 (m, 1 H, ArH), 7.10–7.14 (m, 1 H, ArH), 7.20–7.29 (m, 6 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.74 (d, *J* = 8.4 Hz, 2 H, ArH), 7.81–7.87 (m, 2 H, ArH), 8.34 (dd, *J* = 8.0 Hz, *J*′ = 1.2 Hz, 1 H, ArH), 8.39 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.0, 22.5, 31.0, 31.6, 35.8, 66.7, 116.9, 117.3, 118.3, 120.3, 120.9, 123.0, 125.8, 125.9, 126.5, 127.3, 127.7, 128.1, 128.5, 129.2, 130.3, 132.3, 132.9, 134.9, 143.1, 143.2, 144.6, 147.0, 148.4, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{34}H_{30}N_3O$ $[M + H]^+$: 496.2383; found: 496.2380.

6-(4-Methoxyphenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3l)

Yield: 200 mg (88%); pale yellow solid; mp 241–242 °C.

IR (KBr): 3067, 2954, 2925, 1683, 1606, 1589, 1560, 1509, 1474, 1465, 1420, 1394, 1329, 1314, 1247, 1175, 1045, 923, 835, 797, 694 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 3.83 (s, 3 H, OCH_3), 6.36 (d, *J* = 8.4 Hz, 1 H, CH), 6.71 (d, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 6.94 (d, *J* = 8.8 Hz, 2 H, ArH), 7.04 (t, *J* = 8.0 Hz, 1 H, ArH), 7.11 (t, *J* = 7.2 Hz, 1 H, ArH), 7.14 (s, 1 H, ArH), 7.19–7.28 (m, 3 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.77 (d, *J* = 8.4 Hz, 2 H, ArH), 7.85 (t, *J* = 8.0 Hz, 2 H, ArH), 8.34 (d, *J* = 7.6 Hz, 1 H, ArH), 8.39 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 55.4, 66.7, 114.6, 115.9, 117.3, 118.3, 120.3, 121.0, 123.0, 125.8, 126.6, 127.3, 127.4, 127.8, 128.0, 128.5, 130.1, 133.0, 133.1, 134.9, 142.7, 143.2, 147.0, 148.4, 160.6, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{22}N_3O_2$ $[M + H]^+$: 456.1707; found: 456.1704.

6-(4-Ethoxyphenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3m)

Yield: 192 mg (82%); pale yellow solid; mp 233–234 °C.

IR (KBr): 3066, 3048, 2951, 1683, 1603, 1560, 1448, 1385, 1271, 1238, 1184, 1157, 1086, 1027, 957, 912, 896, 864, 802, 746 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.43 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.03–4.09 (m, 2 H, OCH_2), 6.37 (d, *J* = 8.0 Hz, 1 H, CH), 6.71 (d, *J* = 7.6 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 6.93 (d, *J* = 8.8 Hz, 2 H, ArH), 7.02–7.06 (m, 1 H, ArH), 7.09–7.14 (m, 2 H, ArH), 7.19 (s, 1 H, ArH), 7.21–7.25 (m, 2 H, ArH), 7.49–7.53 (m, 1 H, ArH), 7.75 (d, *J* = 8.4 Hz, 2 H, ArH), 7.81–7.87 (m, 2 H, ArH), 8.34 (dd, *J* = 8.0 Hz, *J*′ = 1.6 Hz, 1 H, ArH), 8.38 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.8, 63.6, 66.7, 115.0, 115.7, 117.3, 118.3, 120.3, 120.9, 123.0, 125.8, 126.6, 127.2, 127.3, 127.8, 127.9, 128.5, 130.1, 133.0, 133.1, 134.9, 142.8, 143.3, 147.0, 148.4, 160.1, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{31}H_{24}N_3O_2$ $[M + H]^+$: 470.1863; found: 470.1871.

2,10-Dichloro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3n)

Yield: 214 mg (87%); pale yellow solid; mp 257–258 °C.

IR (KBr): 3071, 2950, 2925, 2854, 1682, 1609, 1587, 1558, 1474, 1326, 1276, 1247, 1197, 1179, 1153, 1050, 948, 882, 773, 698 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.28 (d, *J* = 8.8 Hz, 1 H, CH), 6.67 (d, *J* = 0.8 Hz, 1 H, ArH), 7.00 (dd, *J* = 8.8 Hz, *J*′ = 2.4 Hz, 1 H, ArH), 7.16 (s, 1 H, ArH), 7.24–7.26 (m, 3 H, ArH), 7.41–7.46 (m, 3 H, ArH), 7.55–7.59 (m, 1 H, ArH), 7.78–7.81 (m, 2 H, ArH), 7.88–7.90 (m, 2 H, ArH), 8.34 (d, *J* = 2.4 Hz, 1 H, ArH), 8.39 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.2, 116.9, 118.6, 119.7, 120.3, 123.5, 125.9, 126.9, 127.0, 127.2, 127.3, 127.4, 128.0, 129.0, 129.3, 129.8, 131.2, 131.9, 132.8, 134.1, 134.5, 135.2, 141.2, 143.0, 145.4, 148.0, 160.4.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{18}Cl_2N_3O$ $[M + H]^+$: 494.0821; found: 494.0812.

3,9-Dichloro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3o)

Yield: 197 mg (80%); pale yellow solid; mp 249–250 °C.

IR (KBr): 3055, 2951, 1679, 1601, 1584, 1485, 1448, 1429, 1340, 1291, 1272, 1240, 1194, 1155, 1043, 1030, 937, 821, 768, 695 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.31 (d, *J* = 2.0 Hz, 1 H, CH), 6.64 (d, *J* = 8.0 Hz, 1 H, ArH), 6.88 (dd, *J* = 8.4 Hz, *J*′ = 1.6 Hz, 1 H, ArH), 7.12 (dd, *J* = 8.0 Hz, *J*′ = 2.0 Hz, 1 H, ArH), 7.17 (s, 1 H, ArH), 7.21 (s, 1 H, ArH), 7.32 (d, *J* = 1.6 Hz, 1 H, ArH), 7.43–7.48 (m, 3 H, ArH), 7.51–7.55 (m, 1 H, ArH), 7.81–7.87 (m, 4 H, ArH), 8.28 (d, *J* = 8.4 Hz, 1 H, ArH), 8.37 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.4, 116.9, 117.1, 117.2, 120.2, 121.9, 124.4, 126.0, 126.2, 126.9, 127.4, 127.8, 128.3, 128.65, 128.74, 129.4, 130.1, 133.9, 134.2, 134.7, 135.1, 139.3, 143.7, 143.9, 145.9, 148.1, 160.5.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{18}Cl_2N_3O$ $[M + H]^+$: 494.0821; found: 494.0814.

2,9-Dichloro-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3p)

Yield: 195 mg (79%); pale yellow solid; mp 282–283 °C.

IR (KBr): 3049, 2996, 2935, 1678, 1585, 1559, 1510, 1473, 1431, 1342, 1329, 1307, 1294, 1251, 1213, 1161, 1135, 1110, 1028, 936, 845, 786, 754, 697 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.31 (s, 1 H, CH), 6.68 (s, 1 H, ArH), 6.88 (d, *J* = 8.8 Hz, 1 H, ArH), 7.17 (s, 1 H, ArH), 7.24–7.26 (m, 3 H, ArH), 7.41–7.46 (m, 3 H, ArH), 7.52–7.56 (m, 1 H, ArH), 7.80–7.81 (m, 2 H, ArH), 7.85–7.86 (m, 2 H, ArH), 8.29 (d, *J* = 8.4 Hz, 1 H, ArH), 8.38 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 66.3, 117.0, 117.17, 117.24, 120.1, 121.9, 123.5, 125.8, 127.0, 127.4, 127.5, 127.9, 128.8, 129.1, 129.4, 129.9, 131.17, 132.01, 133.9, 134.6, 135.2, 139.3, 142.8, 143.7, 145.8, 148.1, 160.5.

HRMS (APCI): *m*/*z* calcd for $C_{29}H_{18}Cl_2N_3O$ [M + H]$^+$: 494.0821; found: 494.0812.

9-Chloro-6-(4-methoxyphenyl)isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3q)

Yield: 210 mg (86%); pale yellow solid; mp >300 °C.

IR (KBr): 3068, 2921, 2852, 1675, 1607, 1591, 1567, 1490, 1465, 1448, 1389, 1335, 1325, 1304, 1280, 1251, 1220, 1183, 1133, 1082, 1017, 953, 907, 886, 692 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.85 (s, 3 H, OCH_3), 6.34 (d, *J* = 2.0 Hz, 1 H, CH), 6.70 (d, *J* = 7.6 Hz, 1 H, ArH), 6.84 (dd, *J* = 8.4 Hz, *J*′ = 2.0 Hz, 1 H, ArH), 6.96 (d, *J* = 8.8 Hz, 2 H, ArH), 7.11–7.15 (m, 2 H, ArH), 7.18 (s, 1 H, ArH), 7.26–7.30 (m, 2 H, ArH), 7.50–7.54 (m, 1 H, ArH), 7.75 (d, *J* = 8.8 Hz, 2 H, ArH), 7.83–7.84 (m, 2 H, ArH), 8.27 (d, *J* = 8.4 Hz, 1 H, ArH), 8.38 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 55.4, 66.7, 114.7, 116.3, 116.9, 117.2, 120.3, 121.5, 122.9, 126.1, 126.7, 126.8, 127.3, 127.4, 127.7, 128.1, 128.6, 128.7, 130.1, 132.9, 135.0, 139.1, 142.2, 144.3, 146.3, 148.2, 160.6, 160.8.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{21}ClN_3O_2$ [M + H]$^+$: 490.1317; found: 490.1301.

2-Chloro-13-methyl-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3r)

Yield: 194 mg (82%); pale yellow solid; mp 253–254 °C.

IR (KBr): 3050, 2996, 2913, 1678, 1603, 1584, 1559, 1510, 1485, 1430, 1341, 1293, 1250, 1212, 1175, 1160, 1135, 1110, 1027, 935, 845, 785, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.78 (s, 3 H, CH_3), 6.33 (d, *J* = 8.0 Hz, 1 H, CH), 6.69–6.70 (m, 1 H, ArH), 6.91 (t, *J* = 7.6 Hz, 1 H, ArH), 7.04 (t, *J* = 7.6 Hz, 1 H, ArH), 7.18 (s, 1 H, ArH), 7.22 (s, 3 H, ArH), 7.38–7.43 (m, 4 H, ArH), 7.70 (d, *J* = 7.2 Hz, 1 H, ArH), 7.81 (d, *J* = 7.6 Hz, 2 H, ArH), 8.24 (d, *J* = 8.0 Hz, 1 H, ArH), 8.40 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 17.5, 66.3, 116.7, 117.2, 118.8, 120.1, 121.3, 123.5, 125.0, 125.9, 126.4, 127.2, 127.5, 128.8, 129.2, 129.6, 131.4, 132.2, 132.9, 134.3, 134.6, 135.6, 136.5, 142.6, 143.3, 145.2, 146.7, 161.0.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{21}ClN_3O$ [M + H]$^+$: 474.1368; found: 474.1373.

6-(4-Methoxyphenyl)-13-methylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3s)

Yield: 190 mg (81%); pale yellow solid; mp 277–278 °C.

IR (KBr): 3062, 2958, 1679, 1622, 1605, 1590, 1573, 1559, 1492, 1464, 1447, 1391, 1339, 1326, 1307, 1276, 1241, 1210, 1166, 1147, 1132, 1049, 915, 871, 823, 762, 750, 693 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.77 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.36 (d, *J* = 8.4 Hz, 1 H, CH), 6.72 (d, *J* = 7.2 Hz, 1 H, ArH), 6.87 (t, *J* = 7.6 Hz, 1 H, ArH), 6.94 (d, *J* = 8.8 Hz, 2 H, ArH), 7.03 (t, *J* = 8.0 Hz, 1 H, ArH), 7.09–7.14 (m, 2 H, ArH), 7.18 (s, 1 H, ArH), 7.21–7.28 (m, 2 H, ArH), 7.39 (t, *J* = 7.6 Hz, 1 H, ArH), 7.68 (d, *J* = 7.2 Hz, 1 H, ArH), 7.76 (d, *J* = 8.8 Hz, 2 H, ArH), 8.23 (d, *J* = 8.0 Hz, 1 H, ArH), 8.39 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 17.4, 55.4, 66.7, 114.6, 115.8, 117.2, 118.7, 120.2, 120.9, 123.0, 125.0, 125.8, 126.2, 127.3, 127.4, 127.5, 127.9, 128.4, 130.2, 132.8, 133.1, 135.4, 136.3, 142.7, 143.1, 145.7, 146.8, 160.3, 161.1.

HRMS (APCI): *m*/*z* calcd for $C_{31}H_{24}N_3O_2$ [M + H]$^+$: 470.1863; found: 470.1885.

3-Chloro-15-methyl-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3t)

Yield: 201 mg (85%); pale yellow solid; mp >300 °C.

IR (KBr): 2949, 2920, 2851, 1671, 1606, 1593, 1567, 1509, 1490, 1476, 1463, 1391, 1325, 1313, 1300, 1246, 1217, 1175, 1132, 1108, 1077, 951, 888, 773, 695 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.55 (s, 3 H, CH_3), 6.33 (d, *J* = 8.4 Hz, 1 H, CH), 6.67 (s, 1 H, ArH), 6.91 (t, *J* = 7.2 Hz, 1 H, ArH), 7.04 (t, *J* = 7.6 Hz, 1 H, ArH), 7.18 (s, 1 H, ArH), 7.23 (s, 3 H, ArH), 7.37–7.44 (m, 3 H, ArH), 7.68 (d, *J* = 8.4 Hz, 1 H, ArH), 7.78 (d, *J* = 8.4 Hz, 1 H, ArH), 7.83 (d, *J* = 7.2 Hz, 2 H, ArH), 8.18 (s, 1 H, ArH), 8.34 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.4, 66.3, 116.7, 117.2, 118.5, 119.9, 121.3, 123.5, 125.9, 126.8, 127.2, 127.4, 127.7, 128.8, 129.2, 129.6, 131.4, 132.2, 132.8, 134.3, 134.6, 136.6, 137.1, 142.6, 143.4, 145.8, 146.3, 160.6.

HRMS (APCI): *m*/*z* calcd for $C_{30}H_{21}ClN_3O$ [M + H]$^+$: 474.1368; found: 474.1385.

13,14-Dimethyl-6-phenylisoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-17(18a*H*)-one (3u) Yield: 188 mg (83%); pale yellow solid; mp >300 °C.

IR (KBr): 3051, 2932, 1674, 1610, 1591, 1574, 1560, 1511, 1489, 1474, 1432, 1396, 1336, 1271, 1244, 1179, 1158, 1132, 1025, 955, 856, 810, 761, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.51 (s, 3 H, CH_3), 2.72 (s, 3 H, CH_3), 6.34 (d, *J* = 8.0 Hz, 1 H, CH), 6.72 (d, *J* = 7.6 Hz, 1 H, ArH), 6.88 (t, *J* = 7.6 Hz, 1 H, ArH), 7.03 (t, *J* = 7.6 Hz, 1 H, ArH), 7.13 (t, *J* = 7.6 Hz, 1 H, ArH), 7.21–7.34 (m, 5 H, ArH), 7.38–7.44 (m, 3 H, ArH), 7.84 (d, *J* = 7.2 Hz, 2 H, ArH), 8.15 (d, *J* = 8.4 Hz, 1 H, ArH), 8.40 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.1, 21.1, 66.6, 117.2, 117.8, 118.2, 118.8, 120.9, 123.1, 124.2, 125.9, 126.0, 127.3, 128.4, 128.5, 128.7, 129.2, 129.3, 130.6, 132.6, 132.8, 134.2, 135.0, 143.0, 143.9, 145.4, 146.4, 161.2.

HRMS (APCI): *m*/*z* calcd for $C_{31}H_{24}N_3O$ [M + H]$^+$: 454.1914; found: 454.1908.

4-Phenylbenzo[7,8]isoquinolino[2,1-*a*]quinazolino[3,2-*c*]quinazolin-15(16a*H*)-one (3v)

Yield: 207 mg (87%); pale yellow solid; mp 288–289 °C.

IR (KBr): 3058, 2893, 2776, 1682, 1608, 1589, 1573, 1560, 1499, 1473, 1400, 1360, 1323, 1313, 1247, 1209, 1187, 1154, 1092, 1036, 936, 894, 773, 760, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.37 (d, *J* = 8.4 Hz, 1 H, CH), 6.83–6.88 (m, 2 H, ArH), 7.00 (t, *J* = 8.0 Hz, 1H, ArH), 7.39 (s, 1 H, ArH), 7.42–7.49 (m, 4 H, ArH), 7.53 (t, *J* = 7.6 Hz, 1 H, ArH), 7.59 (t, *J* = 7.6 Hz, 1 H, ArH),

7.65 (d, J = 8.4 Hz, 1 H, ArH), 7.77 (d, J = 8.0 Hz, 1 H, ArH), 7.83–7.89 (m, 2 H, ArH), 7.95–7.97 (m, 3 H, ArH), 8.29 (d, J = 8.4 Hz, 1 H, ArH), 8.34 (d, J = 8.0 Hz, 1 H, ArH), 8.41 (d, J = 7.6 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 67.2, 114.0, 117.2, 118.4, 120.4, 120.7, 121.2, 122.6, 126.1, 126.2, 126.7, 126.9, 127.36, 127.39, 127.8, 128.1, 128.76, 128.79, 128.8, 129.1, 129.3, 129.6, 133.0, 133.5, 135.0, 135.1, 142.9, 143.4, 147.0, 148.4, 161.0.

HRMS (APCI): m/z calcd for $C_{33}H_{22}N_3O$ [M + H]$^+$: 476.1757; found: 476.1775.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611808.

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