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Note

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Preparation of Quinazolinoquinazolinones *via* a Cascade Approach

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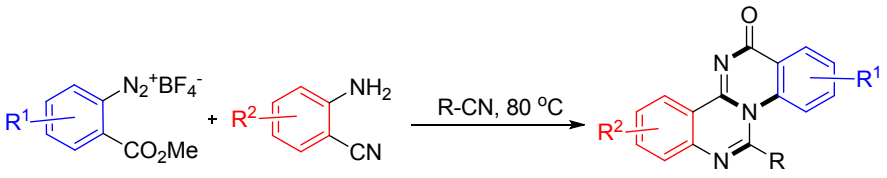
Graphic Abstract (TOC)

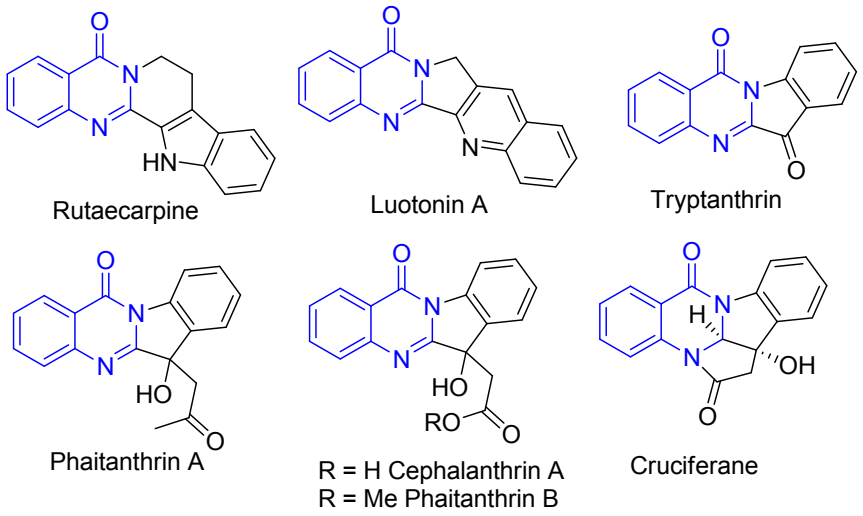


ABSTRACT. A one-pot synthesis of quinazolino[3,4-*a*]quinazolin-13-ones has been realized from the direct reaction of *o*-(methoxycarbonyl)benzenediazonium salts, nitriles and 2-cyanoanilines in moderate to good yields. This method utilizes the *in situ* generation of reactive *N*-arylnitrilium ion, which undergoes further amination/tandem cyclization/amidation to deliver the desired polycyclic scaffolds with consecutive formation of four N-C bonds. Flexibility in substitution patterns, mild reaction conditions and operational simplicity are the salient features of this methodology.

KEYWORDS. Quinazolinoquinazolinone, Diazonium, Cascade reaction, nitrilium.

The polynuclear *N*-heterocyclic compounds with fused multi-ring skeletons are not only of considerable interest to the drug and dye industry but also of great importance in the realm of biological sciences.[1] Especially, the combination of rigid scaffolds with unique installation of functional groups, has evoked special interest in synthetic organic chemistry. Among the various *N*-heterocycles, quinazolin-4(3*H*)-one fused polycyclic frameworks are privileged owing to their prevalence in several natural products such as, Luotonin A,[2] Rutaecarpine,[3] Tryptanthrin,[4] Cephalanthrin A,[5] Phaitanthrin (A and B)[6] and Cruciferane[7] (Scheme 1). On the other hand, quinazolino[3,4-*a*]quinazolin-13-one is particularly fascinating motif due to its ubiquitous structural features.[8] Yet, despite the inspiring skeletal diversity, synthetic efforts towards quinazolino-quinazolinone remain largely underdeveloped.

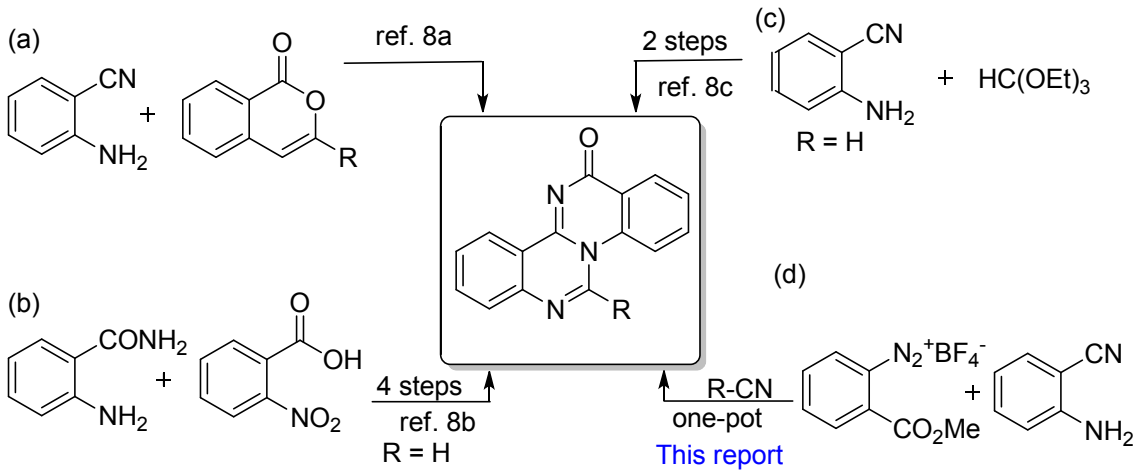
Scheme 1. Quinazolinone Fused Polycyclic Natural Products



In 1984, Yamada *et al*. described the synthesis of 13*H*-quinazolino[3,4-*a*]quinazolin-13-ones from benzoxazine-4-ones and 2-cyanoanilines at elevated temperature (Scheme 2a).[8a] In this preparation, 4-iminoquinazoline is believed to be the key intermediate. Venkateswarlu's group demonstrated a four step synthesis from 2-aminobenzamide and 2-nitrobenzoic acid (Scheme

2b), in which the key intermediate dihydro-13*H*-quinazolino(3,4-*a*)quinazolin-13-one was converted into quinazolino-quinazolinones upon the oxidative aromatization.[8b] In addition, synthesis of 6-unsubstituted analogue was reported by Proença and co-workers involving the acid mediated two step reaction of 2-cyanoanilines with triethylorthoformate (Scheme 2c), where the title compound was obtained by the hydrolysis of the corresponding imine-acid salts.[8c] Finally, Nanni's group observed a minor formation of 6-unsubstituted 13*H*-quinazolino[3,4-*a*]quinazolin-13-one in the multi-step reaction of 2-[4-imino-2-thioxa-1,4-dihydro-3(2*H*)-quinazolinyl]benzonitrile with $Mn(OAc)_3$.[8d] These existing synthetic routes require multi-step procedures, complicated pre-functionalized sites and harsh conditions. Thus, development of a strategically unique approach that can directly deliver fused quinazolino-quinazolinones from readily available substrates in one-step remains elusive.

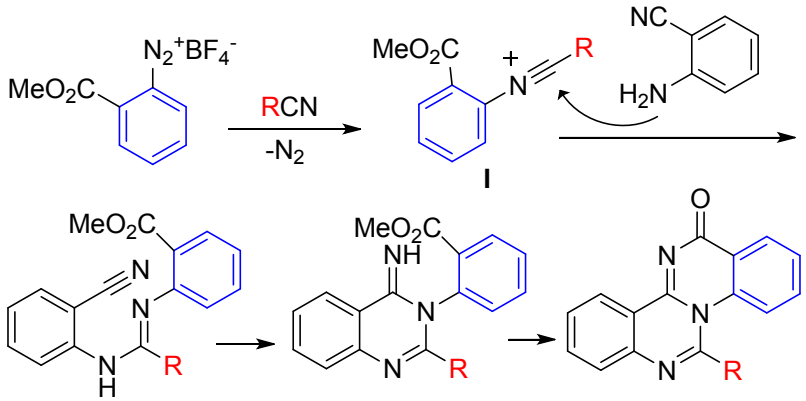
Scheme 2. Various Approaches Towards Quinazolino-quinazolinones.



Aryldiazonium salts are undoubtedly one of the most important precursors due to their widespread applications in organic synthesis.[9] Ease of preparation from a wide range of commercially available anilines, excellent leaving group ability of N_2 and inherent electrophilicity render these compounds an attractive alternative to aromatic halides. Notably,

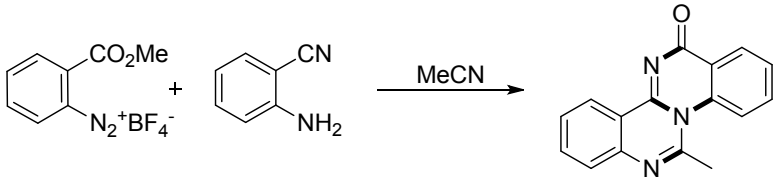
synthetic applications involving *in situ* generation of nitrilium intermediate from aryldiazonium salts and nitriles has gained extensive attention owing to their versatile reactivity and synthetic flexibility.[10] Based on our recent developments on aryldiazonium salts based tandem annulations,[11] we envisaged whether an *in situ* generation of suitably functionalized *N*-arylnitrilium intermediate could be utilized to achieve a mild approach of quinazolino-quinazolin-13-ones, via an intermolecular cascade/tandem cyclization process. Indeed, as a proof-of-concept, recently we developed a synthesis of functionalized quinazolin-4(3*H*)-imines via an annulation protocol.[11b] This strategy led us to envision that further advancements might be plausible by utilizing aryldiazonium precursors. Herein, we disclose a convenient and mild method for the preparation of substituted quinazolino-quinazolinone derivatives from *o*-ester substituted aryldiazonium salts, nitriles and 2-cyanoanilines *via in situ* generation of *N*-arylnitrilium intermediate **I** from the reaction of 2-(methoxycarbonyl)aryldiazonium salt and nitrile followed by a tandem amination/cascade cyclization/amidation to afford the fused quinazolino-quinazolinones (Scheme 3). Substitution reaction of aryldiazonium salts with nitrile components is a known strategy to afford *N*-arylnitrilium intermediates with the loss of N_2 and this intermediate can further undergo reaction with various amino and carbon nucleophiles.[10-11]

Scheme 3. Our Proposed Synthetic Approach



To explore the feasibility, we examined the reaction of **1a** with 2-cyanoaniline (**2a**) in the presence of anhydrous MeCN under various conditions (Table 1). It was observed that, at room temperature, desired product was found only in trace amounts. Guided by our previous learnings,[11a-11d] when the reaction was conducted at 80 °C for 2h, **3a** was isolated in 71% yield (Table 1, entry 2). To our delight, when the reaction was carried out at 80 °C for 5 h, 6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (**3a**) was isolated in 78% yield (Table 1, entry 3). Lowering the reaction temperature with extended time resulted in a diminished yield (Table 1, entry 4). Attempts to reduce the quantity of nitrile in the presence of other co-solvents such as, DMSO, DMF and DCE were unfruitful and led to inferior results (Table 1, entries 5-7).

Table 1. Reaction Optimization[a]



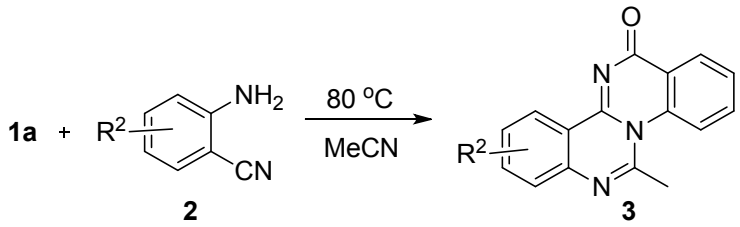
1a **2a** **3a**

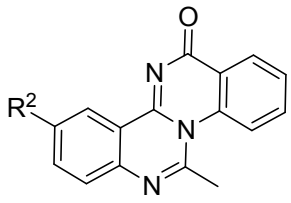
entry	solvent	T (°C)	*t* (h)	Yield[b]
1	MeCN	rt	24	trace
2	MeCN	80	2	71%
3	MeCN	80	5	78%
4	MeCN	50	12	56%
5[c]	MeCN/dmso	80	12	ND[d]
6[c]	MeCN/DMF	100	12	ND[d]
7[c]	MeCN/DCE	reflux	12	ND[d]

[a] Reaction conditions: a mixture of **1a** (0.40 mmol), **2a** (0.48 mmol) and acetonitrile (2 mL) in a sealed tube. [b] yields given refer to isolated yields. [c] MeCN (1 mL) in solvent (2 mL). [d] ND = not detected.

With these optimal conditions in hand, we then systematically studied the scope of this reaction with varieties of substituted 2-cyanoanilines in combination with benzenediazonium salt (**1a**) and acetonitrile (Table 2). Regardless of the position, various halogenated 2-cyanoanilines were participated in the reaction and provided the corresponding products in good isolated yields (Table 2, **3a**-**3d**). Remarkably, anthralonitirle bearing *ortho*-chloro substituent readily reacted (Table 2, **3g**). All these halogenated quinazolino-quinazolinones could serve as potential building blocks for further synthetic conversions. Substrates with phenyl and 1-naphthyl substituents smoothly participated in the transformation and afforded the respective arylated product in good yields (Table 2, **3e**-**3f**). In particular, 2-amino-5-(naphthalen-1-yl)benzonitrile reacted with **1a** in acetonitrile, providing 6-methyl-10-(α-naphthyl)quinazolino[3,4-*a*]quinazolinones **3f** in 73% yield. It is noted that, antharalonitrile with diketo functionality did not led to the desired product (Eq. 1). Heteroaromatic counterparts such as, 2-aminonicotinonitrile, 2-aminothiophene-3-carbonitrile and linear 3-aminocrotononitrile were failed to give the corresponding products despite our extensive efforts.

Table 2. Reaction of **1a** with various 2-cyanoanilines in MeCN[a]





3a, R^2 = H (78%)

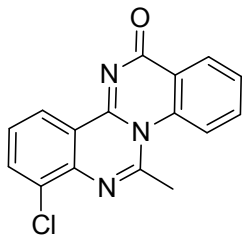
3b, R^2 = Cl (66%)

3c, R^2 = Br (68%)

3d, R^2 = I (66%)

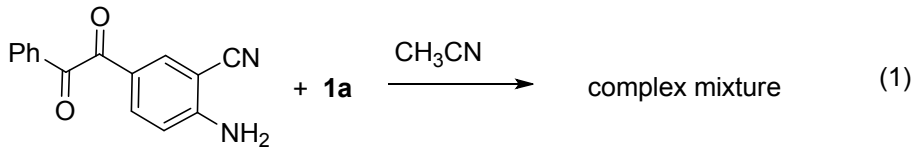
3e, R^2 = *o*-MeC_6H_4 (76%)

3f, R^2 = α-naphthyl (73%)



3g (83%)

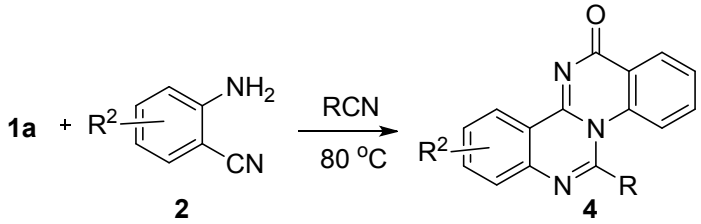
[a] Reaction conditions: **1a** (0.40 mmol) and **2** (1.2 eq) in acetonitrile (2 mL) were heated to 80 °C for 5 h; isolated yields are reported in brackets.

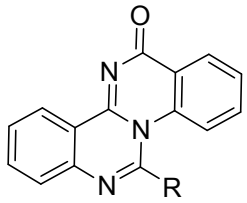


Next, we studied the scope and limitation of this method with various nitrile components (Table 3). A series of aliphatic nitriles such as, 1°, 2°, 3° and cyclic nitriles were involved in the reaction efficiently, leading to the formation of **4a**-**4d** in moderate to excellent yields. Similarly, profound flexibility can be exerted concerning aryl nitriles; thus, variously substituted benzonitriles were utilized in this reaction to furnish 6-arylsubstituted quinazolino-quinazolinones in yields ranging from 54%-63% (Table 3, **4e**-**4g**). The sensitive cyano functionality on the alkyl linkage remains intact, thus offering ample potential for further

synthetic elaboration. To our delight, benzylnitrile was also amenable in this reaction to deliver the corresponding 6-benzylated product in good yields (Table 3, **4i**). Again, reaction of **1a** with 2-amino-5-(naphthalen-1-yl)benzonitrile in various nitriles yielded the corresponding products in good yields (Table 3, **4j**-**4k**). Intriguingly, when 2-amino-5-(naphthalen-1-yl)benzonitrile was treated with benzylnitrile, a mixture of isomers **4l** and **4l'** were formed as an inseparable mixture, presumably due to the similar stability of conjugation. Unfortunately, thiophene-2-carbonitrile and α-chloroacetonitirle were failed to give the corresponding products.

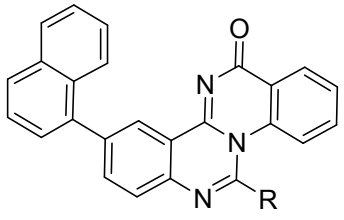
Table 3. Reaction of Various Nitriles with **1a** and **2**[a]





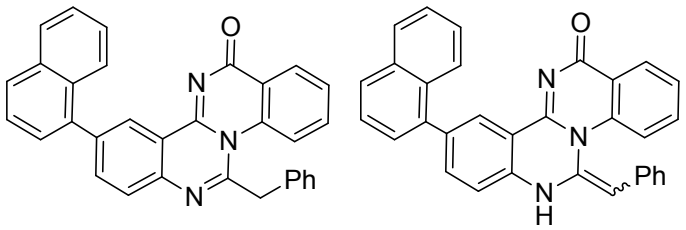
R^2 = H

4a, R = Pr, (76%)
4b, R = *i*-Pr, (47%)
4c, R = *t*-Bu, (42%)
4d, R = *c*-Pr, (69%)
4e, R = Ph, (63%)
4f, R = *o*-Tol, (57%)
4g, R = *p*-Tol, (54%)
4h, R = $NC(CH_2)_4$, (79%)
4i, R = $PhCH_2$, (74%)



R^2 = α-naphthyl

4j, R = Pr, (66%)
4k, R = *i*-Pr, (62%)

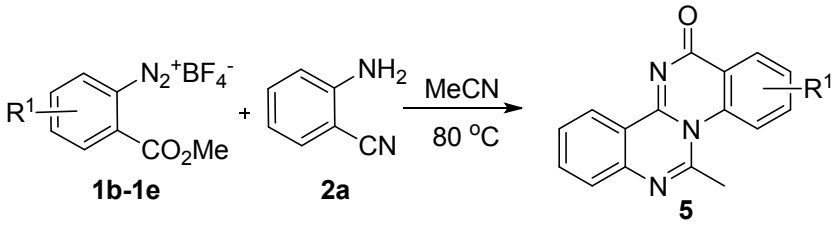


4l + **4l'** (63%) (insepearable 1:0.47)

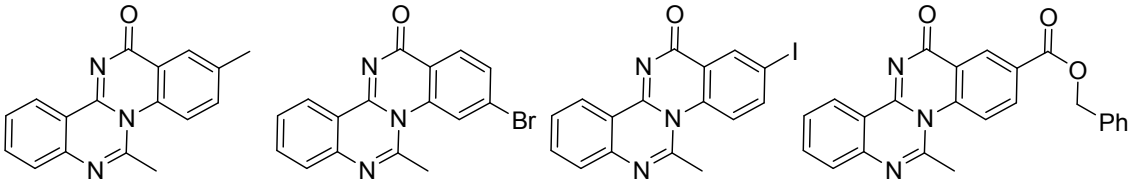
[a] Reaction conditions: **1a** (0.40 mmol) and **2** (1.2 eq) in nitrile (2 mL) were heated to 80 °C for 5 h; isolated yields are reported in brackets.

Finally, we contemplated the scope of this tandem process with variously substituted *o*-(methoxycarbonyl)benzenediazonium salts **1b-1e** (Table 4). The efficiency was slightly affected by variations of substituents on the aryl ring. A series of aryldiazonium salts bearing substituents at *para* and *meta* positions underwent the reaction smoothly to provide the corresponding 13*H*-quinazolino(3,4-*a*)quinazolin-13-ones in acceptable yields (Table 4, **5a**-**5c**) with the exception of 3,4-dimethoxy substituted precursor **1f** (Eq. 2). To further challenge, we also tested the reaction in presence of a functionality of benzyl ester and found that the reaction proceeded smoothly to give **5d** in 44% yield (Table 4, **5d**).

Table 4. Reaction Scope of Aryldiazonium Salts[a]

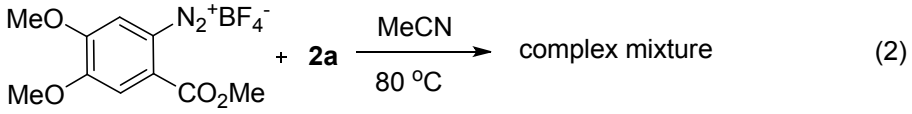


1b-1e **2a** **5**



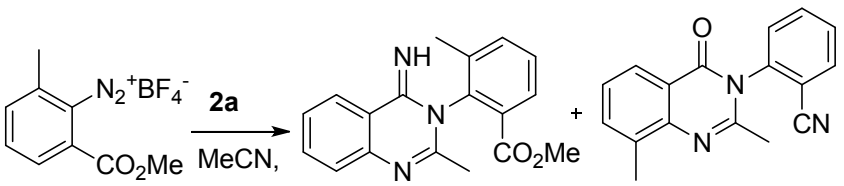
5a (63%) **5b** (36%) **5c** (33%) **5d** (44%)

[a] Reaction conditions: aryldiazonium salt **1** (1.0 eq) and **2** (1.2 eq) in acetonitrile (2 mL) were heated to 80 °C for 5 h; isolated yields are given in brackets.



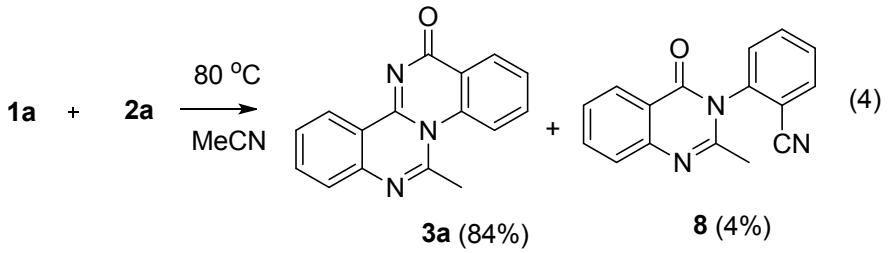
1f (2)

Intriguingly, when 2-(methoxycarbonyl)-6-methylbenzenediazonium salt (**1g**) bearing an adjacent methyl group was employed in this reaction, we observed the formation of quinazolin-4-(3*H*)-imine (**6**) and *N*-arylquinazolin-3-(4*H*)-one (**7**), instead of the corresponding product, 4,6-dimethyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one probably owing to the steric reason (Eq. 3).



1g **6** (73%) **7** (8%) (3)

For a practical utility of this method, a gram scale synthesis of **3a** was performed. Typically, treatment of **1a** (1 g) with anthralonitrile **2a** (0.52 g) in acetonitrile (20 mL) furnished **3a** (0.87 g, 84%) and 2-(2-methyl-4-oxo-quinazolin-3(4*H*)-yl)benzonitrile (**8**) in 4% yield (Eq. 4). (Caution: *Aryldiazonium salts are dangerously explosive upon heating, and reactions must be carried out using necessary precautions*).



In summary, we have developed a unique transition-metal free strategy for accessing diverse polycyclic quinazolino-quinazolinones scaffolds from a simple set of readily available precursors through an intermolecular amination/tandem cyclization/amidation of *in situ* generated *N*-arylnitrilium intermediate from the reaction of diazonium salt with a nitrile functionality. The salient features of this report include mild reaction condition, broad substrate scope, experimental simplicity and consecutive formation of four C-N bonds, making this approach with potential for further synthetic applications.

Experimental Section

General information. ^{1}H and ^{13}C NMR were recorded in a 400 MH_Z spectrometer in $CDCl_3$ and CD_3CN referenced to TMS. All the nitriles were dried over activated 4A^o molecular sieves and solid nitriles were purchased and used without any further drying. All the anilines were commercially purchased and used for diazotization without further purification. Other chemicals were used as purchased. Flash chromatography was performed using silica gel 230-400 mesh. Aryldiazonium salts were prepared according to the literature procedure. In cases of known compounds, their spectral data were compared with the literature values. Melting points were determined on a Fargo MP-1D instrument. Unless otherwise noted, all the reactions were performed without any special precautions. Compounds **2b**,[12a] **2c**,[12b] **2d**,[12c], 2g,[12d] and **2h**[12e] were prepared according to the literature methods, whereas the preparation of **2e** and **2f** were achieved by a Suzuki coupling.[12b]

General procedure for preparing aryldiazonium tetrafluoroborate.

Methyl-2-aminobenzoate (1g, 6.61 mmol, 1.0 equiv.) was dissolved in a mixture of water (4 mL) and 50% aqueous hydrofluroboric acid (2.4 mL, 13.23 mmol, 2.0 equiv.). The mixture was cooled to 0 ^{o}C and a solution of $NaNO_2$ (0.46 g, 6.68 mmol in 4 mL of water) was added slowly. The resulting reaction mixture was stirred at 0 ^{o}C for 30 minutes and the precipitate was collected by filtration. The solid product was dissolved in minimum acetone and re-precipitated using diethyl ether to yield 2-(methoxycarbonyl)benzenediazonium tetrafluoroborate which was dried under vacuum. (white solid, 1.45 g, 88%). The spectral data are in agreement with the literature reported.[13]

2-(Methoxycarbonyl)-4-methylbenzenediazonium tetrafluoroborate (1b).

901 mg, 94%, pale pink solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.81 (d, J = 8.4 Hz, 1H), 8.27 (s, 1H), 8.06 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H), 2.64 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 161.5, 154.3, 135.5, 135.2, 133.0, 130.4, 111.8, 54.0, 22.1; HRMS (ESI-TOF) calcd. For $C_9H_9N_2O_2$ $(M\text{-}BF_4)^+$ m/z = 177.0659, found 177.0667.

5-Bromo-2-(methoxycarbonyl)benzenediazonium tetrafluoroborate (1c).

630 mg, 74%, brown solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.27 (s, 1H), 8.61 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 160.9, 143.7, 136.8, 133.3, 129.5, 126.9, 117.3, 54.3; HRMS (ESI-TOF) calcd. For $C_8H_6{}^{79}BrN_2O_2$ $(M\text{-}BF_4)^+$ m/z = 240.9607, found 240.9612; HRMS (ESI-TOF) calcd. For $C_8H_6{}^{81}BrN_2O_2$ $(M\text{-}BF_4)^+$ m/z = 242.9587, found 242.9595.

4-Iodo-2-(methoxycarbonyl)benzenediazonium tetrafluoroborate (1d).

569 mg, 84%, white solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.70 (d, J = 8.4 Hz, 2H), 8.58 (d, J = 8.0 Hz, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 160.4, 143.9, 140.7, 135.0, 130.4, 114.6, 113.6, 54.2; HRMS (ESI-TOF) calcd. For $C_8H_6IN_2O_2$ $(M\text{-}BF_4)^+$ m/z = 288.9468, found 288.9474.

4-((Benzyloxy)carbonyl)-2-(methoxycarbonyl)benzenediazonium tetrafluoroborate (1e).

770 mg, 72%, off-white solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.53 (s, 1H), 8.81 (d, *J* = 7.6 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 6.8 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 3H), 5.46 (s, 2H), 4.05 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 161.8, 160.8, 140.8, 135.5, 135.0, 134.8, 133.5, 132.8, 128.6 (2C), 128.5, 117.0, 68.0, 54.4; HRMS (ESI-TOF) calcd. For $C_{16}H_{13}N_2O_4$ (M-BF_4)$^+$ m/z = 297.0870, found 297.0880.

4,5-Dimethoxy-2-(methoxycarbonyl)benzenediazonium tetrafluoroborate (1f).

677 mg, 77%, brown solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 7.79 (s, 1H), 4.13 (s, 3H), 4.00 (s, 3H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 161.2, 158.2, 151.6, 127.5, 115.7, 114.4, 104.0, 57.9, 57.3, 53.9; HRMS (ESI-TOF) calcd. For $C_{10}H_{11}N_2O_4$ (M-BF_4)$^+$ m/z = 223.0713, found 223.0724.

2-(Methoxycarbonyl)-6-methylbenzenediazonium tetrafluoroborate (1g).

870 mg, 91%, white solid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.27 (d, *J* = 4.8 Hz, 2H), 8.13 (t, *J* = 4.8 Hz, 1H), 4.03 (s, 3H), 2.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 161.6, 146.9, 140.2, 136.7, 130.4, 130.3, 115.0, 54.1, 18.4; HRMS (ESI-TOF) calcd. For $C_9H_9N_2O_2$ (M-BF_4)$^+$ m/z = 177.0659, found 177.0663.

General Procedure for the synthesis of 13*H*-quinazolino[3,4-*a*]quinazolin-13-ones.

In a dry 10 mL glass sealed tube, aryldiazonium salt (0.40 mmol) and 2-cyanoaniline (0.48 mmol) were suspended in 2 mL of anhydrous nitrile. The tube was sealed with a Teflon screw cap and heated in an oil bath (80 ^{o}C) for 5h. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (30 mL) and washed with saturated aq. $NaHCO_3$ solution (10 mL). Organic Layer was dried over anhydrous Na_2SO_4. Solvents removed and purified by column chromatography (Eluent 40% to 70% EtOAc:Hexane) to obtain the desired compounds.

6-Methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3a).[8b]

81 mg, 78%, pale yellow solid: mp 227-229 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.32 (d, *J* = 7.6 Hz, 1H), 7.76 (ddd, *J* = 15.4, 7.6, 1.6 Hz, 1H), 7.72 (d, *J* = 3.2 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.61-7.57 (m, 1H), 7.51 (ddd, *J* = 15.2, 7.6, 0.8 Hz, 1H), 2.95 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 153.2, 148.2, 143.3, 136.7, 134.8, 131.9, 128.2, 128.1, 128.0, 126.7, 126.1, 122.9, 120.4, 119.7, 26.0; HRMS (ESI-TOF) calcd. For $C_{16}H_{12}N_3O$ $(M+H)^+$ m/z = 262.0980, found 262.0984.

10-Chloro-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3b).

94 mg, 81%, off-white solid: mp 228-229 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.4 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 3.6 Hz, 2H), 7.68 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.62-7.57 (m, 2H), 2.95 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.9, 152.1, 148.5, 141.7, 136.5, 135.1, 133.9, 132.0, 128.4, 128.3, 127.8, 125.9, 122.9, 120.8, 120.4, 26.1; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{35}ClN_3O$ $(M+H)^+$ m/z = 296.0591, found 296.0599; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{37}ClN_3O$ $(M+H)^+$ m/z = 298.0561, found 298.0624.

10-Bromo-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3c).

92 mg, 68%, white solid: mp 273-274 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 2.0 Hz, 1H), 8.38 (d, *J* = 7.6 Hz, 1H), 7.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.77-7.72 (m, 2H), 7.64 (ddd, *J* = 13.8, 6.6, 2.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 2.96 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.9, 152.0, 148.8, 141.9, 138.0, 136.5, 132.1, 129.2, 128.5 (2C), 127.8, 123.1, 121.9, 121.1, 120.4, 26.0; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{79}BrN_3O$ $(M+H)^+$ m/z = 340.0085, found 340.0086; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{81}BrN_3O$ $(M+H)^+$ m/z = 342.0065, found 342.0073.

10-Iodo-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3d).

101 mg, 66%, white solid: mp 234-235 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, *J* = 2.0 Hz, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.06 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.77-7.71 (m, 2H), 7.67-7.63 (m, 1H), 7.43-7.42 (m, 1H), 2.96 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.0, 151.8, 148.8,

143.6, 142.6, 136.6, 135.4, 132.1, 128.5 (2C), 127.8, 123.1, 121.2, 120.4, 92.8, 26.1; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}IN_3O$ $(M+H)^+$ m/z = 387.9947, found 387.9961.

6-Methyl-10-(*o*-tolyl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3e).

106 mg, 76%, off-white solid: mp 119-120 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 2.0 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 7.77 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.74-7.70 (m, 3H), 7.65-7.59 (m, 1H), 7.27-7.23 (m, 4H), 2.99 (s, 3H), 2.26 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 153.3, 148.0, 142.2, 140.0, 136.7, 136.1 (2C), 135.1, 131.9, 130.4, 129.8, 128.3, 128.1, 127.9, 126.8, 125.9 (2C), 123.0, 120.3, 119.6, 26.0, 20.4; HRMS (ESI-TOF) calcd. For $C_{23}H_{18}N_3O$ $(M+H)^+$ m/z = 352.1450, found 352.1457.

6-Methyl-10-(naphthalen-1-yl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3f).

113 mg, 73%, off-white solid: mp 283-284 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 2.0 Hz, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 7.95 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.89 (t, *J* = 8.4 Hz, 2H), 7.81-7.71 (m, 4H), 7.62 (ddd, *J* = 13.4, 6.4, 2.4 Hz, 1H), 7.54-7.50 (m, 1H), 7.49-7.46 (m, 2H), 7.41 (t, *J* = 8.0 Hz, 1H), 3.01 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 153.3, 148.2, 142.5, 141.0, 138.2, 136.9, 136.7, 133.7, 131.9, 131.2, 128.4 (2C), 128.3, 128.2, 127.6, 127.5, 126.4, 126.0, 125.9, 125.3 (2C), 123.0, 120.3, 119.9, 26.1; HRMS (ESI-TOF) calcd. For $C_{26}H_{18}N_3O$ $(M+H)^+$ m/z = 388.1450, found 388.1454.

8-Chloro-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (3g).

97 mg, 83%, off-white solid: mp 233-234 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.33 (d, *J* = 7.6 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.75-7.72 (m, 2H), 7.64-7.60 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 3.01 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.0, 152.6, 149.3, 140.1, 136.5, 134.9, 132.1, 130.9, 128.4, 128.3, 128.0, 125.4, 122.9, 121.5, 120.4, 26.2; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{35}ClN_3O$ $(M+H)^+$ m/z = 296.0591, found 296.0599; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{37}ClN_3O$ $(M+H)^+$ m/z = 298.0561, found 298.0602.

6-Propyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4a).

87 mg, 76%, pale yellow solid: mp 238-239 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.36 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.82-7.78 (m, 1H), 7.74-7.66 (m, 3H), 7.62 (ddd, *J* = 14.8, 7.4, 1.2 Hz, 1H), 7.55 (ddd, *J* = 15.2, 7.4, 1.2 Hz, 1H), 3.19 (t, *J* = 7.6 Hz, 2H), 1.91 (sex, *J* = 7.6 Hz, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.5, 153.3, 151.9, 143.5, 136.7, 134.8, 131.8, 128.3, 128.1, 128.0, 126.7, 126.5, 123.1, 120.4, 119.7, 39.0, 22.3, 13.6; HRMS (ESI-TOF) calcd. For $C_{18}H_{16}N_3O$ $(M+H)^+$ m/z = 290.1293, found 290.1291.

6-Isopropyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4b).

54 mg, 47%, brown solid: mp 178-179 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.32 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.77 (ddd, *J* = 11.6, 7.4, 1.2 Hz, 1H), 7.75-7.67 (m, 2H), 7.60-7.55 (m, 2H), 7.51 (ddd, *J* = 14.4, 7.0, 1.2 Hz, 1H), 3.74 (hept, *J* = 6.4 Hz, 1H), 1.39 (d, *J* = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.5, 157.2, 153.3, 143.7, 136.7, 134.7, 131.7, 128.1, 127.9, 127.8, 126.6, 126.5, 123.0, 120.2, 119.5, 33.5, 22.3; HRMS (ESI-TOF) calcd. For $C_{18}H_{16}N_3O$ $(M+H)^+$ m/z = 290.1293, found 290.1290.

6-(*tert*-Butyl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4c).

51 mg, 42%, brown sticky solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.22 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.77 (ddd, *J* = 15.2, 7.6, 1.6 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.63-7.52 (m, 3H), 7.50-7.48 (m, 1H), 1.42 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 159.4, 154.3, 143.5, 138.5, 134.7, 130.7, 127.9, 127.7, 127.3, 126.5, 126.2, 122.3, 122.0, 119.2, 42.6, 32.0; HRMS (ESI-TOF) calcd. For $C_{19}H_{18}N_3O$ $(M+H)^+$ m/z = 304.1450, found 304.1441.

6-Cyclopropyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4d).

81 mg, 69%, brown solid: mp 195-196 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.37 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.77-7.68 (m, 2H), 7.62-7.57 (m, 2H), 7.48 (t, *J* = 8.0 Hz, 1H), 2.34 (hept, *J* = 4.8 Hz, 1H), 1.68-1.64 (m, 2H), 1.30-1.26 (m,

2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 167.6, 153.2, 153.0, 143.8, 136.9, 134.7, 131.5, 128.2, 127.9, 127.3, 126.8, 126.2, 123.0, 120.7, 119.6, 17.4, 13.4; HRMS (ESI-TOF) calcd. For $C_{18}H_{14}N_3O$ $(M+H)^+$ m/z = 288.1137, found 288.1136.

6-Phenyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4e).

80 mg, 63%, off-white solid: mp 143-144 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 8.0 Hz, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 3.6 Hz, 2H), 7.61-7.57 (m, 3H), 7.50-7.44 (m, 1H), 7.43-7.39 (m, 3H), 7.26-7.22 (m, 1H), 7.96 (d, *J* = 8.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 167.6, 153.6, 149.3, 143.7, 137.6, 135.5, 135.0, 131.1, 131.0, 129.1, 128.6, 128.5, 127.8, 127.5, 127.4, 126.8, 122.3, 121.9, 119.9; HRMS (ESI-TOF) calcd. For $C_{21}H_{14}N_3O$ $(M+H)^+$ m/z = 324.1137, found 324.1136.

6-(*o*-Tolyl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4f).

76 mg, 57%, off-white solid: mp 274-275 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.0, 0.8 Hz, 1H), 8.32 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.87-7.81 (m, 2H), 7.62 (ddd, *J* = 11.2, 4.8, 2.0 Hz, 1H), 7.50 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.45-7.37 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.23-7.19 (m, 2H), 6.95 (d, *J* = 8.8 Hz, 1H), 2.12 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 153.2, 149.4, 143.5, 137.3, 135.7, 135.0 (2C), 131.6, 131.4, 130.7, 129.3, 128.7, 127.9, 127.7, 127.3, 127.0 (2C), 122.3, 120.3, 120.0, 19.6; HRMS (ESI-TOF) calcd. For $C_{22}H_{16}N_3O$ $(M+H)^+$ m/z = 338.1293, found 338.1292.

6-(*p*-Tolyl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4g).

73 mg, 54%, pale yellow solid: mp 226-227 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75-8.72 (m, 1H), 8.29-8.27 (m, 1H), 7.82-7.80 (m, 2H), 7.59-7.55 (m, 1H), 7.50-7.48 (m, 2H), 7.43 (ddd, *J* = 15.0, 7.4, 1.2 Hz, 1H), 7.28-7.24 (m, 1H), 7.21-7.19 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 153.7, 149.5, 143.8, 141.7, 137.7, 135.0, 132.7,

130.9, 129.8, 128.5, 128.4, 127.7, 127.5, 127.3, 126.8, 122.2, 121.9, 119.9, 21.5; HRMS (ESI-TOF) calcd. For $C_{22}H_{16}N_3O$ $(M+H)^+$ m/z = 338.1293, found 338.1294.

5-(13-Oxo-13*H*-quinazolino[3,4-*a*]quinazolin-6-yl)pentanenitrile (4h).

104 mg, 79%, pale yellow sticky solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.33 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.81-7.77 (m, 1H), 7.72 (ddd, *J* = 15.6, 8.0, 1.6 Hz, 1H), 7.69 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.65-7.59 (m, 2H), 7.54 (ddd, *J* = 15.2, 7.8, 1.2 Hz, 1H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 2.12-2.04 (m, 2H), 1.73-1.66 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.3, 153.1, 150.6, 143.2, 136.4, 134.9, 132.0, 128.3, 128.2 (2C), 126.6, 126.5, 123.1, 120.3, 119.6, 119.1, 36.2, 27.5, 24.7, 17.0; HRMS (ESI-TOF) calcd. For $C_{20}H_{17}N_4O$ $(M+H)^+$ m/z = 329.1402, found 329.1397.

6-Benzyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4i).

101 mg, 74%, pale yellow solid: mp 208-209 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.0 Hz, 1H), 8.32 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.83-7.74 (m, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.65 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.61-7.54 (m, 2H), 7.29-7.20 (m, 5H), 4.55 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.3, 153.4, 149.9, 143.4, 136.7, 135.4, 134.8, 131.9, 128.9, 128.5, 128.4, 128.3, 128.2, 127.4, 126.8, 126.7, 122.9, 120.6, 119.8, 42.7; HRMS (ESI-TOF) calcd. For $C_{22}H_{15}N_3O$ $(M+H)^+$ m/z = 338.1293, found 338.1297.

10-(Naphthalen-1-yl)-6-propyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4j).

109 mg, 66%, pale yellow solid: mp 212-213 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 2.0 Hz, 1H), 8.33 (d, *J* = 7.2 Hz, 1H), 7.93 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.88 (t, *J* = 8.4 Hz, 2H), 7.82-7.79 (m, 2H), 7.71-7.67 (m, 2H), 7.61-7.58 (m, 1H), 7.52 (d, *J* = 7.2 Hz, 1H), 7.49-7.45 (m, 2H), 7.42-7.38 (m, 1H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.92 (sex, *J* = 7.2 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.4, 153.2, 152.0, 142.6, 140.8, 138.2, 136.8, 136.7, 133.7, 131.8, 131.1, 128.3 (2C), 128.2, 128.0, 127.5, 127.4, 126.4, 126.3, 125.9, 125.3, 125.2,

123.0, 120.4, 119.7, 39.0, 22.3, 13.5; HRMS (ESI-TOF) calcd. For $C_{28}H_{22}N_3O$ $(M+H)^+$ m/z = 416.1763, found 416.1761.

6-Isopropyl-10-(naphthalen-1-yl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4k).

102 mg, 62%, pale brown solid: mp 126-127 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 2.0 Hz, 1H), 8.33 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.93 (d, *J* = 8.0, 1.6 Hz, 1H), 7.83 (t, *J* = 8.8 Hz, 2H), 7.85-7.80 (m, 2H), 7.73-7.69 (m, 1H), 7.61-7.58 (m, 2H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.47-7.44 (m, 2H), 7.42-7.38 (m, 1H), 3.80 (hept, *J* = 6.8 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.5, 157.4, 153.3, 142.9, 140.8, 138.2, 136.8 (2C), 133.7, 131.8, 131.2, 128.3 (2C), 128.1, 127.9, 127.5, 127.4, 126.5, 126.4, 125.8, 125.3, 125.2, 123.1, 120.3, 119.6, 33.6, 22.4; HRMS (ESI-TOF) calcd. For $C_{28}H_{22}N_3O$ $(M+H)^+$ m/z = 416.1763, found 416.1760.

6-Benzyl-10-(naphthalen-1-yl)-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4l) and 6-benzylidene-10-(naphthalen-1-yl)-6,7-dihydro-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (4l').

116 mg, 63% (**4l : 4l'** = 1: 0.47), pale yellow solid: mp 132-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 2.0 Hz, 1H), 8.28 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.95 (dd, *J* = 8.0, 2.0 Hz, 1.52 H), 7.89 (d, *J* = 8.4 Hz, 1.52 H), 7.87-7.85 (m, 2H), 7.82-7.79 (m, 2H), 7.77-7.72 (m, 1H), 7.74-7.70 (m, 0.90 H), 7.57 (ddd, *J* = 15.0, 7.2, 0.8 Hz, 1H), 7.53-7.45 (m, 2H), 7.44-7.41 (m, 2H), 7.40-7.37 (m, 2H), 7.35-7.31 (m, 1H), 7.29-7.26 (m, 3.5 H), 7.25-7.23 (m, 2.36H), 7.12 (t, *J* = 7.2 Hz, 0.47 H), 6.25 (brs, 0.79 H), 4.59 (s, 2H), 4.20 (s, 0.94 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.2, 165.1, 161.8, 153.3, 150.0, 142.6, 141.2, 138.6, 138.4, 138.1, 136.9, 136.7, 135.6, 135.5, 133.7, 133.6, 131.9, 131.2, 131.1, 129.3, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.5, 127.4, 127.2, 126.5, 126.46, 126.40, 126.3, 125.9, 125.4, 125.3, 123.0, 122.8, 120.6, 119.8, 112.4, 45.5, 42.8; HRMS (ESI-TOF) calcd. For $C_{32}H_{22}N_3O$ $(M+H)^+$ m/z = 464.1763, found 464.1766.

2,6-Dimethyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (5a).

65 mg, 63%, brown solid: mp 224-225 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 8.0 Hz, 1H), 8.16 (s, 1H), 7.79-7.76 (m, 1H), 7.67-7.60 (m, 2H), 7.55-7.51 (m, 2H), 2.95 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.4, 153.0, 148.2, 143.3, 138.6, 134.7, 134.5, 132.9, 128.0 (2C), 126.7, 126.1, 122.8, 120.2, 119.8, 26.1, 20.9; HRMS (ESI-TOF) calcd. For $C_{17}H_{14}N_3O$ $(M+H)^+$ m/z = 276.1137, found 276.1144.

3-Bromo-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (5b).

37 mg, 36%, brown solid: mp 248-249 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 1.6 Hz, 1H), 7.81 (ddd, *J* = 15.2, 7.4, 1.2 Hz, 1H), 7.80-7.75 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 2.97 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.7, 153.5, 147.6, 143.2, 137.5, 135.2, 131.6, 129.9, 128.3, 126.8, 126.6, 126.4, 123.3, 121.7, 119.6, 26.0; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{79}BrN_3O$ $(M+H)^+$ m/z = 340.0085, found 340.0086; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}{}^{81}BrN_3O$ $(M+H)^+$ m/z = 342.0065, found 342.0081.

2-Iodo-6-methyl-13*H*-quinazolino[3,4-*a*]quinazolin-13-one (5c).

34 mg, 33%, brown solid: mp 152-153 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 2.0 Hz, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8.01 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 2.95 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8, 153.3, 147.6, 143.3, 140.6, 137.2, 136.2, 135.2, 128.3, 126.9, 126.3, 124.2, 121.9, 119.6, 93.0, 26.0; HRMS (ESI-TOF) calcd. For $C_{16}H_{11}IN_3O$ $(M+H)^+$ m/z = 387.9947, found 387.9961.

Benzyl 6-methyl-13-oxo-13*H*-quinazolino[3,4-*a*]quinazoline-2-carboxylate (5d).

34 mg, 33%, brown sticky solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.0 Hz, 1H), 8.49 (s, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.83-7.79 (m, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.45-7.41 (m, 2H), 7.39-7.33 (m, 3H), 5.41 (s, 2H), 2.98 (s, 3H);

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 164.6, 153.8, 147.9, 143.4, 136.6, 135.2, 135.1, 133.2, 128.8, 128.7 (2C), 128.5, 128.4, 128.3, 126.8, 126.4, 125.7, 122.1, 119.5, 67.8, 26.0; HRMS (ESI-TOF) calcd. For $C_{24}H_{18}N_3O_3$ $(M+H)^+$ m/z = 396.1348, found 396.1362.

Methyl 2-(4-imino-2-methylquinazolin-3(4*H*)-yl)-3-methylbenzoate (6).

85 mg, 73%, off-white solid: mp 95-96 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.07 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.69 (ddd, *J* = 15.4, 7.6, 1.6 Hz, 1H), 7.66-7.64 (m, 1H), 7.61-7.53 (m, 2H), 7.45 (ddd, *J* = 15.0, 7.6, 0.8 Hz, 1H), 5.07 (brs, 1H), 3.68 (s, 3H), 2.18 (s, 3H), 2.05 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 164.6, 155.8, 152.4, 144.9, 137.5, 136.4, 135.4, 134.2, 130.9, 130.3, 128.0, 127.1, 127.0, 125.8, 117.7, 52.6, 23.3, 17.3; HRMS (ESI-TOF) calcd. For $C_{18}H_{18}N_3O_2$ $(M+H)^+$ m/z = 308.1399, found 308.1399.

2-(2,8-Dimethyl-4-oxoquinazolin-3(4*H*)-yl)benzonitrile (7).

9 mg, 8%%, pale yellow solid: mp 254-255 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.87 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.79 (td, *J* = 8.0, 1.6 Hz, 1H), 7.64-7.60 (m, 2H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 2.62 (s, 3H), 2.25 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.1, 150.8, 145.8, 140.7, 135.7, 134.2, 122.9 (2C), 129.8, 129.7, 126.5, 124.7, 120.2, 115.1, 113.2, 23.9, 17.3; HRMS (ESI-TOF) calcd. For $C_{17}H_{14}N_3O$ $(M+H)^+$ m/z = 276.1137, found 276.1139.

2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzonitrile (8).[14]

42 mg, 4%, brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.86 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.81-7.75 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 2.24 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.5, 152.5, 147.0, 140.3, 135.1, 134.3, 133.9, 130.0, 129.6, 127.1, 126.9 (2C), 120.2, 114.9, 113.2, 23.5; HRMS (ESI-TOF) calcd. For $C_{16}H_{12}N_3O$ $(M+H)^+$ m/z = 262.0980, found 262.0981.

ASSOCIATED CONTENT

Supporting Information

Spectra for all new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxx

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Notes

The authors declare no competing financial interest.

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