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Chada Raji Reddy, Anootha Neeliveettil, Uprety Ajaykumar, Nagender Punna, Luc Neuville, et al.. Access to N-Fused Quinazolinones by Radical-Promoted Cascade Annulations of Alkenyl N-Cyanamides with Aromatic Aldehydes. *Journal of Organic Chemistry*, 2024, 89 (10), pp.7115-7124. 10.1021/acs.joc.4c00494 . hal-04733233

HAL Id: hal-04733233

<https://hal.science/hal-04733233v1>

Submitted on 11 Oct 2024

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Access to N-Fused Quinazolinones by Radical-Promoted Cascade Annulations of Alkenyl *N*-Cyanamides with Aromatic Aldehydes

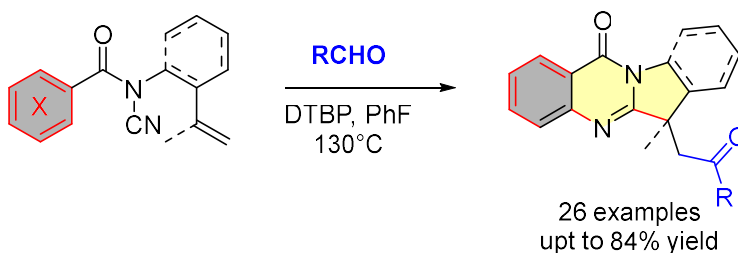
Chada Raji Reddy,^{*, a, b} Anootha Neeliveetil,^{a, b} Uprety Ajaykumar,^{a, b} Nagender Punna,^{a, b}
Luc Neuville^c and Geraldine Masson^c

^aDepartment of Organic Synthesis & Process Chemistry CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500007, India

^bAcademy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

^cInstitut de Chimie des Substances Naturelles (ICSN), CNRS UPR 2301, Université Paris-Saclay, 1 avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France

E-mail: rajireddy@iict.res.in



ABSTRACT: A cascade radical cyclization of alkenyl *N*-cyanamides with aromatic aldehydes has been achieved for an expeditious synthesis of keto-methylated dihydropyrrolo-quinazolinones. Benzoyl radicals, generated from aryl aldehydes in the presence of di-*tert*-butyl peroxide (DTBP), promoted the domino annulations leading to distinctive functionalized quinazolinones in good yields. In addition, the robustness of the present protocol is validated by employing heterocyclic and natural product-based aldehydes. **KEYWORDS:** Radical cyclization • Quinazolines • *N*-cyanamides • Aromatic aldehydes • Domino reaction •

INTRODUCTION

Quinazolinones, with their exceptional bioactivity and therapeutic promise, hold a unique position at the organic chemistry-biology interface.¹ Pyrrolo-quinazolinones (Nfused) are widely distributed in natural alkaloids and pharmaceuticals, establishing them as privileged *aza*-heterocycles (Figure 1).²⁻⁶ For instance, vasicinone derivatives (I to III) are known for their anti-inflammatory, antidepressive, and bronchodilator activities.³ The alkaloid isaindigotone (IV), which was extracted from the root of *Isatis indigotca Fort*, exhibits distinctive antitumor activities and was recently recognized as a novel class of selective ligands for telomeric Gquadruplex DNA.⁴ Additionally, tryptanthrin (V), an indole quinazoline alkaloid, exhibits a broad spectrum of pharmacological activities, including antitubercular, anti-inflammatory, antitumor, antiviral and antimicrobial properties.⁵ Likewise, the thieno[2,3-*d*]pyrimidine (VI) was shown to possess diverse activities, such as antidermatomycosis, anti-inflammatory gastric and antisecretory activities.⁶ Hence, the demand for practical and rapid approaches for the construction of complex and functionalized polycyclic pyrrolo-quinazolinone derivatives continue to provide an impetus in synthetic organic chemistry.⁷ On the other hand, radical cascade cyclization has emerged as a straightforward approach for producing structurally diverse and complex *aza*-heterocycles.^{8,9} In this context, alkenyl *N*-cyanamides have been used as radical acceptors for assembly of polycyclic dihydropyrrolo-quinazolinones.⁹ The alkene and cyano functionalities present in *N*-cyanamide alkenes can be used to generate of an intermediate amido-iminyl radical, and olefin difunctionalization, highlighting their potential for divergent last-stage radical termination or cyclization.^{7,8} This underscores their potential for divergent radical termination or cyclization, making alkenyl *N*-cyanamides a valuable tool for efficiently generating molecular complexity. Various radicals, including alkyl (obtained by oxidative decarbonylation of several secondary and tertiary alkyl aldehydes),^{9a} perfluoroalkyl,^{9b,c} phosphorus,^{9d} 1,3-diketo-methylene^{9e} and arylsulfonyl^{9f} radicals have been employed in these radical-promoted cascade annulations of alkenyl *N*-cyanamides 1a leading to dihydropyrrolo [2,1-*b*]quinazolin-9(1*H*)-one VII (Scheme 1a). Despite these advance, a radical cascade cyclization involving benzoyl radical to access keto-methylated dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-ones has not been reported. Notably, an efficient synthesis of alkyl-substituted quinazolin-9(1*H*)-ones VIII was demonstrated by Wang and co-workers using aliphatic aldehydes as alkyl radical precursors (Scheme 1b).^{9a} However, this method is

limited to aliphatic aldehydes and aromatic aldehydes were not examined. As part of our ongoing research projects on radical cyclizations,¹⁰ we became interested in exploring the use of aryl aldehydes to generate benzoyl radicals for the assembly of keto-methylated 2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-ones. Herein, we present a metal-free benzoyl radical-triggered cascade addition/cyclization reaction of *N*-cyanamide alkenes for a divergent and expedient synthesis of polycyclic pyrrolo-quinazolinones (3) (Scheme 1c). Notably, various aromatic aldehydes, abundant and inexpensive aldehyde feedstocks, are exploited as highly effective radical precursors¹¹ leading to keto-containing pyrrolo-quinazolinones.

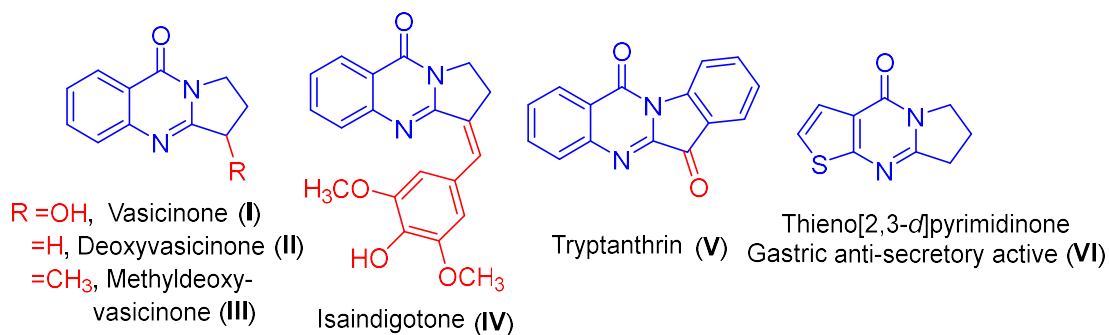
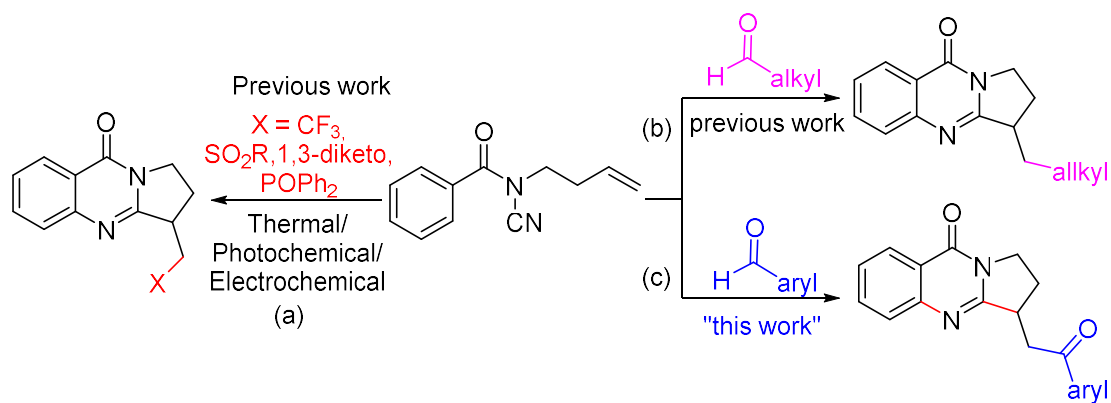


Figure 1. Representative bio-active molecules having pyrrolo-quinazolinone moiety

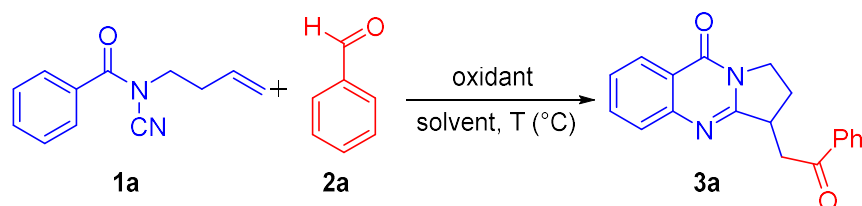


Scheme 1. Radical-promoted annulations of *N*-alkenyl cyanamides to quinazolinones

RESULTS AND DISCUSSION

Our study commenced by using *N*-cyano-*N*-(3-methylbut-3-en-1-yl)benzamide **1a** with benzaldehyde **2a** as model substrates to examine effects of various parameters. In an initial investigation, the reaction was carried out using 3 equiv of DTBP in fluorobenzene at 130 °C and delightfully the corresponding keto quinazolin-9(1*H*)-one (**3a**) was obtained in 68% yield (Table 1, entry 1). Further, solvent screening with toluene, chlorobenzene, acetonitrile, 1,4-dioxane and trifluorotoluene revealed that fluorobenzene was the solvent of choice, affording the desired product **3a** in good yield (Table 1, entry 2 to 6). Next, the other oxidants were studied, wherein the use of TBHP gave a slightly lower yield (Table 1, entry 7), K₂S₂O₈ failed to furnish the product **3a** (Table 1, entry 8). Pleasingly, the yield was substantially increased (80%) in the presence of 5 equiv of DTBP (Table 1, entry 9). Decreasing the reaction temperature to 100 °C led to the formation of **3a** in low yield (Table 1, entry 10). Finally, the cascade radical cyclization did not proceed in the absence of an oxidant (Table 1, entry 11).

Table 1. Optimization of the reaction conditions

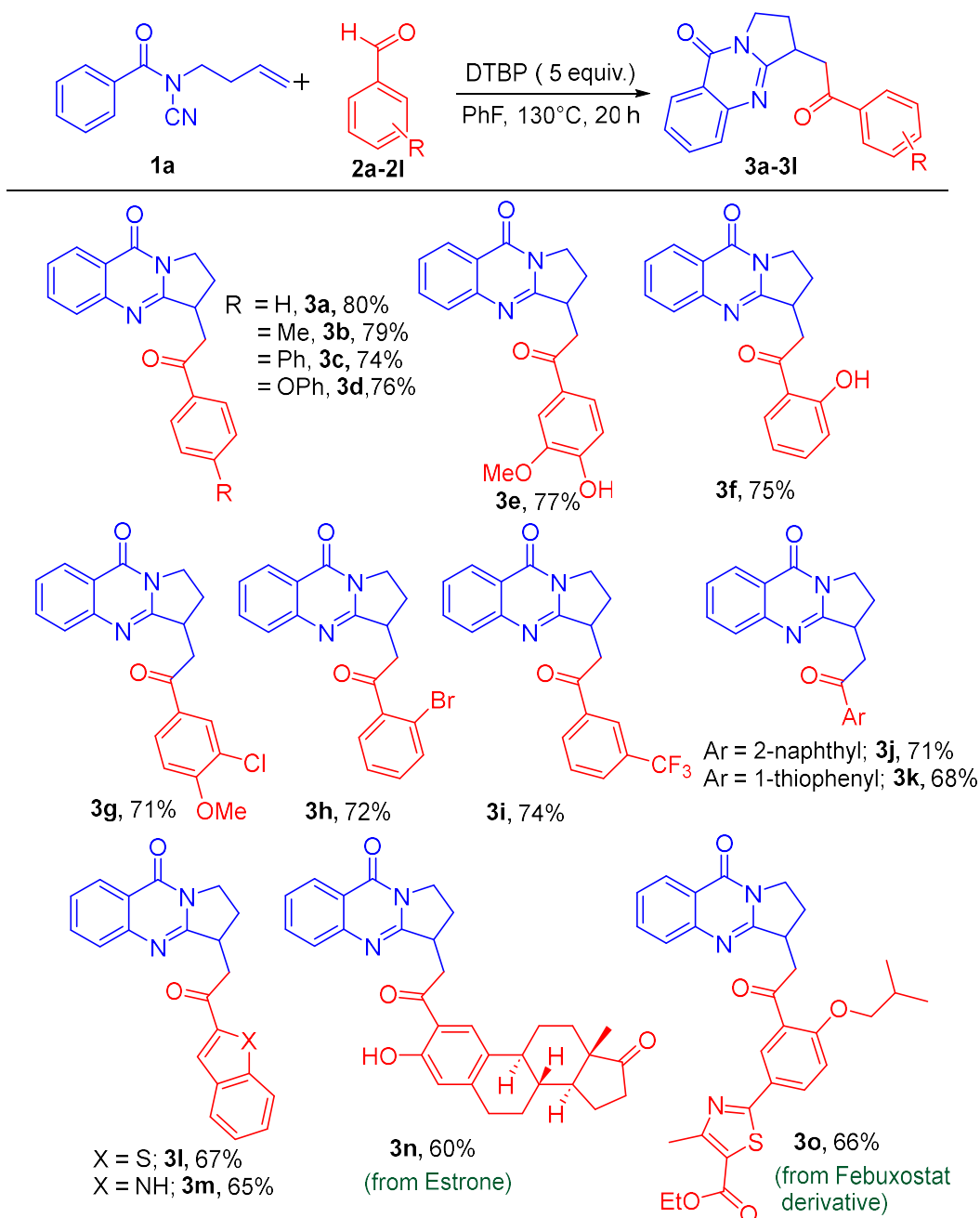


entry	oxidant (equiv.)	solvent	T(°C)	yield ^b (%)
1	DTBP (3)	PhF	130	68
2	DTBP (3)	Toluene	130	43
3	DTBP (3)	PhCl	130	58
4	DTBP (3)	CH ₃ CN	130	-
5	DTBP (3)	1,4-dioxane	130	-
6	TBHP (3)	PhF	130	60
7	K ₂ S ₂ O ₈ (3)	PhF	130	-
8	DTBP (5)	PhF	130	80
9	DTBP (5)	PhF	100	43
10	-	PhF	130	-

^a Unless otherwise stated, all reactions were performed using 0.3 mmol of **1a** with 0.6 mmol of **2a**, 1.5 mmol of DTBP in 3 mL of PhF and stirred for given time at specified temperature;

^b Isolated yield,

Having the optimized reaction conditions in hand, the scope of this DTBP-mediated cascade radical annulation of *N*-cyano-*N*-(3-methylbut-3-en-1-yl)benzamide (**1a**) with a variety of aromatic aldehydes **2** was examined (Scheme 2). Aldehydes having electron-donating groups such as 4-Me (**2b**), 4-Ph (**2c**), and 4-OPh (**2d**) were found to be suitable to deliver the corresponding quinazolin-9(*1H*)-ones **3b** to **3d** in good yields. The substrates having phenolic hydroxy groups also underwent cascade annulations to give the desired products **3e** and **3f** in 77% and 75% yield, respectively. Furthermore, aldehydes with electron-withdrawing groups such as 3-Cl (**2g**), 2-Br (**2h**), and 3-CF₃ (**2i**) were also found to be compatible, furnishing the corresponding keto-methylated quinazolin-9(*1H*)-ones **3g** to **3i** in good yields. A smooth conversion was observed with 2-naphthaldehyde (**2j**) to furnish the quinazolin-9(*1H*)-one **3j** in 71% yield. Likewise, heteroaryl aldehydes such as thiophene (**2k**), benzothiophene (**2l**), and indole (**2m**) aldehydes were also found to be compatible in reaction with **1a** to afford the corresponding quinazolin-9(*1H*)-ones **3k** to **3m** in good yields. It is also worth mentioning that the method can be applied to more complex aldehydes such as the natural product-derived aldehydes estrone (**2n**) and febuxostat (**2o**), which were converted to the corresponding quinazolinones **3n** and **3o** in 60% and 66% yields, respectively (Scheme 2).



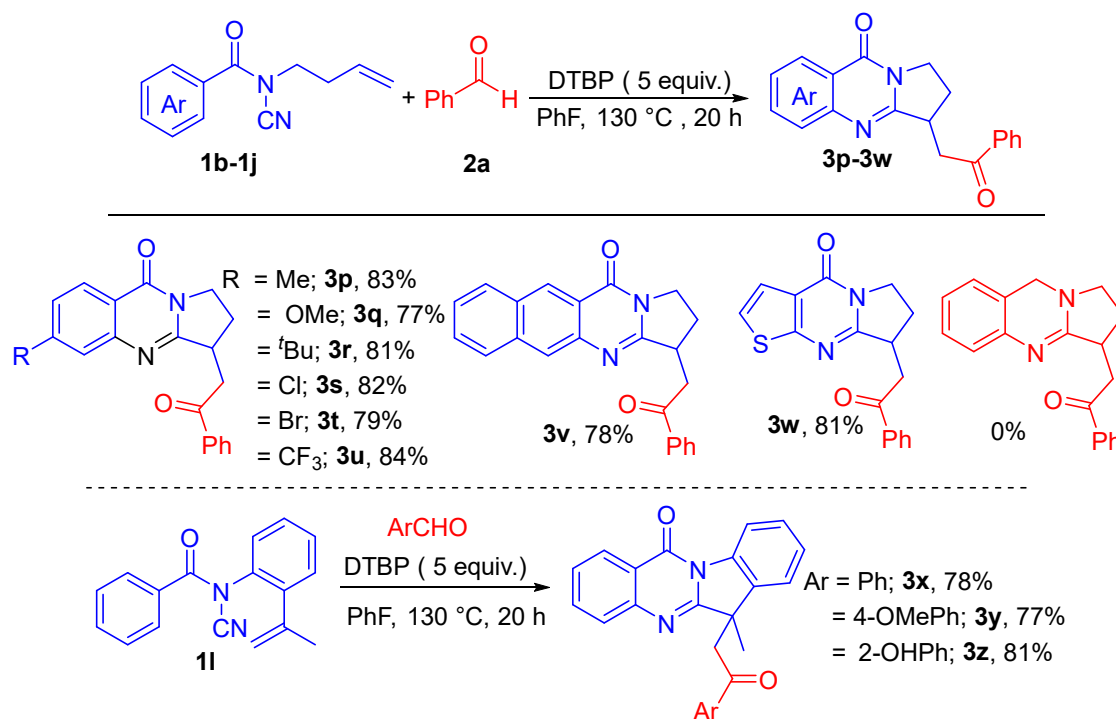
^aUnless otherwise stated, all reactions were performed using 0.3 mmol of **1a** with 0.6 mmol of **2**, oxidant in 3 mL of solvent at 130°C. Isolated yield.

Scheme 2. Substrate scope of aldehydes^a

Afterward, we investigated the substrate scope of *N*-cyano-*N*-(2-(prop-1-en-2-yl)phenyl)benzamide **1** under optimized reaction conditions (Scheme 3). The reactions of *N*-cyano benzamides **1b-1d**, featuring versatile substituents on the phenyl ring such as 4-Me (**1b**), 4-MeO (**1c**) and 4-*t*Bu (**1d**) participated efficiently to afford the required products **3p** to **3r** in good yields. Further, halogen 7-Cl (**1e**), 7-Br (**1f**) and electrowithdrawing group 7-CF₃

(1g) substituted benzoylated alkenyl *N*-cyanamides were well tolerated, furnishing the desired quinazolin-9(1*H*)-ones **3s** to **3u** in significant yields. Next, naphthyl derived *N*-cyanamide also equally participated in the reaction to give benzo[*g*]quinazolin-4(3*H*)-one **3v** in 78% yield. Pleasingly, thiophenyl (heteroaryl) *N*-cyanamide alkene **1h** was also underwent the cascade annulations to provide the dihydropyrrole fused thieno[2,3-*d*]pyrimidin-4(6*H*)-one **3w** (a pharmaceutically active motif)⁶ in 81% yield.

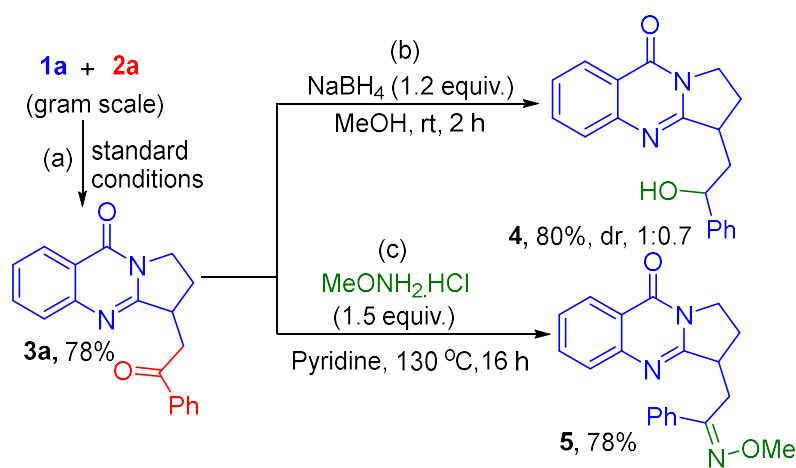
It is important to note that the *N*-cyano benzyl amine **1j** failed to participate in the present benzoyl radical promoted cascade annulation under standard conditions. This suggests that the amide (*N*-benzoyl) group is necessary for the annulation. To further widen the substrate scope, we explored the reactivity of *N*-cyano-*N*-(2 (prop-1-en-2-yl)phenyl)benzamide **1k** with benzaldehyde in the presence of DTBP in fluorobenzene. Delightfully, the expected 6-methyl-6-(2-oxo-2-phenylethyl)indolo[2,1-*b*]quinazolin-12(6*H*)-one **3x**, tetracyclic core of an alkaloid tryptanthrin, was obtained in 78% yield. Further, the reactivity of **1k** was extended to other radicals, generated from anisaldehyde and salicylaldehyde, for the synthesis of tetracyclic tryptanthrin analogues **3y** (77%) and **3z** (81%), respectively.



^aUnless otherwise stated, all reactions were performed using 0.3 mmol of **1a** with 0.6 mmol of **2**, oxidant in 3 mL of solvent at 130 °C. Isolated yield.

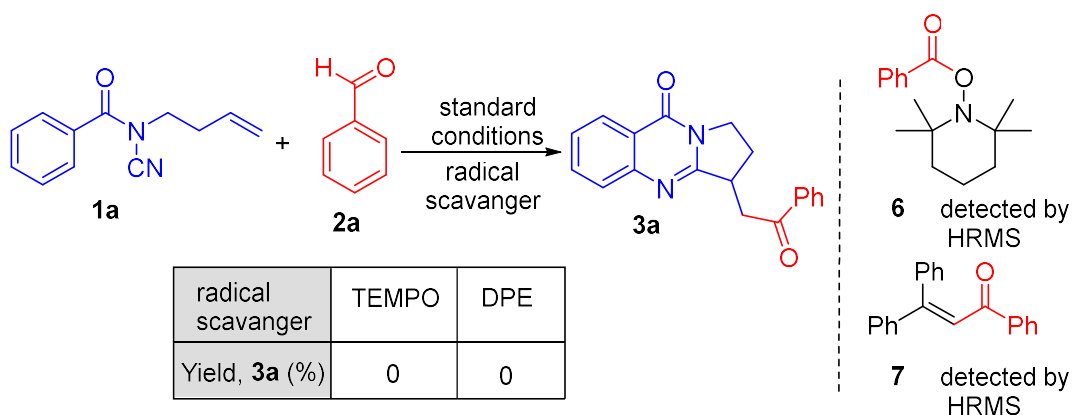
Scheme 3: Substrate scope of *N*-cyanamide alkenes.^a

To showcase the synthetic applicability of the present cascade radical cyclization, a gram-scale reaction of 1a with 2a was fruitfully validated under standard reaction conditions to access quinazolin-9(1*H*)-one 3a in 78% yield (Scheme 4a). Further, the utility of the product was demonstrated by functional group transformations. The carbonyl functionality of 3a was reduced in the presence of NaBH₄ to the alcohol 4 in 80% yield (Scheme 4b). The reaction of 3a with methoxy-amine provided the ketoxime 5 in 78% yield (Scheme 4c).

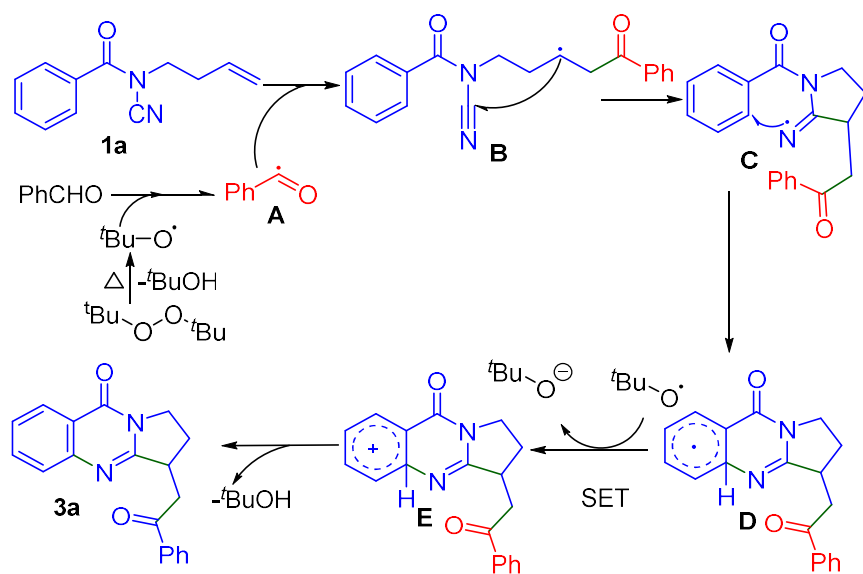


Scheme 4. Gram-Scale synthesis of 3a and Its transformation

To assess the reaction pathway, a few control experiments were performed in the presence of radical scavengers such as 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) and 1,1-diphenylethylene (DPE). It was observed that the reaction was suppressed in both cases generating the TEMPO adduct (6) and DPE adduct (7), as identified by HRMS analysis (Scheme 5). These results are consistent with a radical cyclization pathway.



Scheme 5. Control experiments



Scheme 6. Plausible reaction mechanism.

A plausible mechanism has been proposed based on the literature^{9,12} and the above observed results (Scheme 6). Initially, the in situ generated tert-butoxyl radical under thermal conditions abstracts the aldehyde hydrogen atom to give the benzoyl radical A, which then adds to the unactivated double bond of 1a in regioselectively to form the more stable, secondary radical species B. Subsequently B undergoes a 5-exodig cyclization to produce the imine radical C which adds to an aryl ring to generate the corresponding aryl radical D. A single electron transfer (SET) process leads to the aryl cationic species E, followed by deprotonation, provides the product 3a.

CONCLUSION

In summary, we have demonstrated the DTBP-mediated cascade radical cyclization of alkenyl *N*-cyanamides with aromatic aldehydes, facilitating the facile construction of pyrrolo-quinazolinones with excellent yields. The developed cascade protocol is scalable and exhibits a broader substrate scope, enabling the synthesis of diversely functionalized analogs of bioactive alkaloids such as deoxy-vasicinone and tryptanthrins. Our strategy relies on easily accessible starting materials, employs mild metal-free reaction conditions, and offers valuable synthetic utility.

EXPERIMENTAL SECTION

General information:

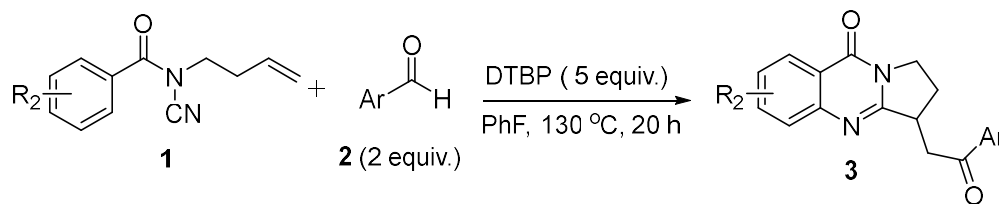
All the reactions were performed in oven-dried glass apparatus. For reactions sensitive to air and moisture, an inert atmosphere (nitrogen) was employed, and freshly distilled anhydrous solvents were used. Commercially available reagents (aldehydes and DTBP) were utilized without additional purification. Thin-layer chromatography performed on silica plates and visualized under UV light and β -naphthol was used to monitor all reactions. Column chromatography, using hexane and ethyl acetate as the eluent, was carried out on silica gel (100–200 mesh). The ^1H NMR spectra were recorded in CDCl_3 at 500 and 400 MHz, while the ^{13}C NMR spectra were recorded at 126 and 101 MHz. δ 7.26 and δ 77 correspond to CDCl_3 in ^1H NMR and ^{13}C NMR, respectively, and δ 1.56 is related to the moisture present in CDCl_3 . Chemical shifts are reported in δ (ppm) relative to TMS as an internal standard, and J values are expressed in Hz. Multiplicity is denoted as s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), etc. High-resolution mass spectra (HRMS) $[\text{ESI}]^+$ were obtained using either a TOF or a double focusing spectrometer. Melting point of all solid compounds was determined using a melting point apparatus.

Procedures for the Preparation of Starting Materials:

All the basic starting materials (**1a-1w**)⁹ and (**11**)¹³ were prepared based on literature reports and the spectral data was compared.

General procedure for the preparation of benzoylated quinazolinones.

General Procedure for the Synthesis of Keto-Containing Pyrroloquinazolinones (**3a to 3z**)



N-Cyano benzamide (0.3 mmol, 1 equiv), aryl aldehyde (0.6 mmol, 2 equiv), and di-*tert*-butyl peroxide (1.5 mmol, 5 equiv.) were taken in a reaction vial, and 3 mL of fluorobenzene was added. The reaction mixture was allowed to stir at 130 °C (oil bath temperature) and upon completion of the reaction (monitored by TLC), the reaction mass was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated, and the crude reaction mixture was purified by column chromatography on silica gel using ethyl acetate and hexanes as an eluent to afford the desired product.

3-(2-Oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**3a**)

Yellow solid, 61 mg, 80% yield, mp 151-153 °C; *R_f* = 0.5 (Ethyl Acetate : Hexane = 1:1); ¹H NMR (500 MHz, CDCl₃) δ 8.31 (dd, *J* = 8.0, 1.3 Hz, 1H), 8.05 – 8.01 (m, 2H), 7.75 – 7.70 (m, 1H), 7.67 – 7.64 (m, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.47 – 7.43 (m, 1H), 4.40 – 4.34 (m, 1H), 4.08 – 4.02 (m, 1H), 3.99 (dd, *J* = 18.2, 3.1 Hz, 1H), 3.93 – 3.85 (m, 1H), 3.38 – 3.30 (m, 1H), 2.79 – 2.72 (m, 1H), 1.97 – 1.87 (m, 1H); ¹³C{¹H}NMR (101 MHz, CDCl₃) δ 197.4, 161.1, 149.2, 136.5, 134.1, 133.5, 130.1, 128.8 (2C), 128.1 (2C),

126.9, 126.5, 126.3, 120.8, 45.1, 41.1, 39.6, 27.2; HRMS (ESI): m/z calcd for C₁₉H₁₆N₂O₂ (M+H)⁺ 305.1285, Found 305.1275.

3-(2-Oxo-2-(p-tolyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3b)

Yellow solid, 63 mg, 79% yield, mp 112-114 °C; R_f = 0.5 (Ethyl Acetate : Hexane = 1:1); ¹H NMR (400 MHz, CDCl₃) δ 8.23 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.68 – 7.62 (m, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.23 – 7.18 (m, 2H), 4.32 – 4.25 (m, 1H), 4.01 – 3.92 (m, 1H), 3.91 – 3.84 (m, 1H), 3.83 – 3.76 (m, 1H), 3.29 – 3.20 (m, 1H), 2.71 – 2.63 (m, 1H), 2.35 (s, 3H), 1.90 – 1.78 (m, 1H); ¹³C{¹H}NMR (101 MHz, CDCl₃) δ 197.1, 161.2, 160.9, 149.1, 144.4, 134.1, 134.1, 129.4 (2C), 128.3 (2C), 126.9, 126.5, 126.3, 120.9, 45.1, 41.1, 39.7, 27.2, 21.7; HRMS (ESI): m/z calcd for C₂₀H₁₉N₂O₂ (M+H)⁺ 319.1441, Found 319.1419.

3-(2-([1,1'-Biphenyl]-4-yl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3c)

White solid, 70 mg, 74% yield, mp 153-155 °C; R_f = 0.6 (Ethyl Acetate : Hexane = 1:1); ¹H NMR (500 MHz, CDCl₃) δ 8.32 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 2H), 7.75 – 7.69 (m, 3H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.65 – 7.60 (m, 2H), 7.50 – 7.44 (m, 3H), 7.4 – 7.39 (m, 1H), 4.41 – 4.35 (m, 1H), 4.10 – 3.99 (m, 2H), 3.95 – 3.88 (m, 1H), 3.33 – 3.41 (m, 1H), 2.82 – 2.72 (m, 1H), 1.99 – 1.88 (m, 1H); ¹³C{¹H}NMR (101 MHz, CDCl₃) δ 197.0, 161.0, 149.2, 146.2, 139.8, 135.2, 134.2, 129.0 (2C), 128.8 (2C), 128.4, 127.4, 127.3, 127.1, 126.9 (2C), 126.5 (2C), 126.3, 120.8, 45.0, 41.2, 39.7, 27.2; HRMS (ESI): m/z calcd for C₂₅H₂₁N₂O₂ (M+H)⁺ 381.1598, Found 381.1611.

3-(2-Oxo-2-(4-Phenoxyphenyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3d)

Pale yellow solid, 75 mg, 76% yield, mp 145-147 °C; R_f = 0.6 (Ethyl Acetate : Hexane = 1:1); ¹H NMR (500 MHz, CDCl₃) δ 8.30 (d, *J* = 7.7 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.68 – 7.61

(m, 2H), 7.45 (t, $J = 7.8$ Hz, 2H), 7.36 (t, $J = 7.9$ Hz, 2H), 7.25 – 7.21 (m, 1H), 7.15 (t, $J = 7.3$ Hz, 1H), 7.02 (d, $J = 7.8$ Hz, 2H), 4.41 – 4.32 (m, 1H), 4.09 – 3.99 (m, 1H), 3.97 – 3.91 (m, 1H), 3.90 – 3.82 (m, 1H), 3.36 – 3.27 (m, 1H), 2.79 – 2.68 (m, 1H), 1.97 – 1.86 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 196.8, 161.0, 160.9, 157.9, 156.5, 149.2, 138.3, 134.2, 130.1, 130.0 (2C), 126.9, 126.5, 126.3, 123.9, 123.7, 122.9, 120.8, 119.2 (2C), 117.9, 45.0, 41.3, 39.6, 27.1; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_3$ (M+H) $^+$ 397.1547, Found 397.1532.
3-(2-(4-Hydroxy-3-methoxyphenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3e)

White solid, 67 mg, 77% yield, mp 188-190 °C; $R_f = 0.3$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (500 MHz, CDCl_3) δ 8.31 (d, $J = 7.6$ Hz, 1H), 7.76 – 7.65 (m, 2H), 7.62 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.55 (d, $J = 1.7$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 6.96 (d, $J = 8.3$ Hz, 1H), 6.31 (s, 1H), 4.43 – 4.34 (m, 1H), 4.12 – 4.03 (m, 1H), 3.95 (s, 3H), 3.94 – 3.84 (m, 2H), 3.46 – 3.32 (m, 1H), 2.79 – 2.68 (m, 1H), 2.01 – 1.88 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 195.9, 161.9, 160.6, 153.5, 150.9, 146.8, 134.5, 129.3, 126.6 (2C), 123.7, 120.6, 114.1 (2C), 109.8, 55.9, 45.6, 40.8, 39.9, 26.8; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_4$ (M+H) $^+$ 351.1339, Found 351.1343.

3-(2-(2-Hydroxyphenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3f)

Yellow solid, 60 mg, 75% yield, mp 130-132 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 12.05 (s, 1H), 8.33 – 8.27 (m, 1H), 7.88 – 7.83 (m, 1H), 7.76 – 7.70 (m, 1H), 7.66 (d, $J = 7.9$ Hz, 1H), 7.53 – 7.43 (m, 2H), 7.04 – 6.99 (m, 1H), 6.96 – 6.90 (m, 1H), 4.44 – 4.34 (m, 1H), 4.11 – 3.99 (m, 2H), 3.95 – 3.83 (m, 1H), 3.44 – 3.33 (m, 1H), 2.81 – 2.69 (m, 1H), 2.02 – 1.88 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 203.4, 162.4, 160.9, 160.6, 149.0, 136.8, 134.2, 129.9, 126.9, 126.5, 126.4, 120.8, 119.3, 119.2, 118.7, 45.0, 40.7, 39.3, 27.1; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_3$ (M+H) $^+$ 321.1234, Found 321.1234.

3-(2-(3-chloro-4-methoxyphenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3g)

Pale yellow solid, 65 mg, 71% yield, mp 108-110 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.31 (dd, $J = 8.0, 1.0$ Hz, 1H), 8.07 (d, $J = 2.1$ Hz, 1H), 7.95 (dd, $J = 8.6, 2.1$ Hz, 1H), 7.76 – 7.69 (m, 1H), 7.65 (d, $J = 7.9$ Hz, 1H), 7.49 – 7.42 (m, 1H), 6.99 (d, $J = 8.7$ Hz, 1H), 4.41 – 4.31 (m, 1H), 4.10 – 4.01 (m, 1H), 3.99 (s, 3H), 3.95 – 3.80 (m, 2H), 3.27 (dd, $J = 17.7, 9.1$ Hz, 1H), 2.80 – 2.68 (m, 1H), 1.98 – 1.84 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 195.1, 161.0, 160.9, 159.1, 149.2, 134.2, 130.5, 130.1, 128.6, 126.9, 126.5, 126.3, 123.1, 120.9, 111.4, 56.5, 44.9, 40.8, 39.6, 27.2; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{18}\text{ClN}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 369.1000, Found 369.0979.

3-(2-(2-Bromophenyl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3h)

Yellow solid, 69 mg, 72% yield, mp 86-88 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (500 MHz, CDCl_3) δ 8.30 (d, $J = 7.2$ Hz, 1H), 7.75 – 7.68 (m, 1H), 7.67 – 7.61 (m, 2H), 7.57 – 7.51 (m, 1H), 7.48 – 7.38 (m, 2H), 7.36 – 7.30 (m, 1H), 4.44 – 4.32 (m, 1H), 4.10 – 3.99 (m, 1H), 3.95 – 3.86 (m, 1H), 3.85 – 3.76 (m, 1H), 3.43 – 3.32 (m, 1H), 2.80 – 2.70 (m, 1H), 2.10 – 1.98 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.5, 160.8, 160.7, 140.9, 134.3, 133.8 (2C), 131.9, 128.7, 127.6, 126.6, 126.5 (2C), 120.7, 118.7, 45.1, 44.8, 39.8, 26.78; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{16}\text{BrN}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 383.0390, Found 383.0377.

3-(2-Oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3i)

Pale yellow solid, 69 mg, 74% yield, mp 120-122 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.30 (d, $J = 9.5$ Hz, 2H), 8.21 (d, $J = 7.4$ Hz, 1H), 7.85 (d, $J = 7.3$ Hz, 1H), 7.76 – 7.69 (m, 1H), 7.65 (d, $J = 7.1$ Hz, 2H), 7.46 (t, $J = 7.2$ Hz, 1H), 4.39 (t, $J = 9.9$ Hz, 1H), 4.12 – 3.85 (m, 3H), 3.56 – 3.33 (m, 1H), 2.84 – 2.70 (m, 1H), 2.02 –

1.88 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 196.2, 160.9, 160.7, 148.9, 136.9, 134.2, 131.7 (q, $J = 33.1$ Hz), 131.3, 129.9 (d, $J = 3.2$ Hz), 129.5, 128.7, 126.5, 126.4, 123.6 (q, $J = 274.1$ Hz), 124.9, 120.8, 45.0, 41.2, 39.4, 27.1; ^{19}F NMR (376 MHz, CDCl_3) δ -62.80; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 373.1158, Found 373.1183.

3-(2-(naphthalen-2-yl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3j)

Yellow solid, 63 mg, 71% yield, mp 130-132 °C; $R_f = 0.6$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (500 MHz, CDCl_3) δ 8.69 (d, $J = 8.5$ Hz, 1H), 8.30 (d, $J = 7.7$ Hz, 1H), 8.02 (d, $J = 6.5$ Hz, 2H), 7.90 (d, $J = 8.0$ Hz, 1H), 7.71 (t, $J = 7.3$ Hz, 1H), 7.65 – 7.59 (m, 2H), 7.58 – 7.49 (m, 2H), 7.45 (t, $J = 7.4$ Hz, 1H), 4.39 (t, $J = 9.6$ Hz, 1H), 4.09 – 3.92 (m, 3H), 3.41 (m, 1H), 2.79 (m, 1H), 2.09 – 1.95 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.5, 161.0, 160.87, 149.2, 135.2, 134.1, 134.0, 133.2, 130.1, 128.5, 128.2, 128.0, 126.9, 126.6, 126.5, 126.3, 125.8, 124.4, 120.8, 45.0, 44.2, 40.1, 27.2; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 355.1441, Found 355.1431.

3-(2-Oxo-2-(thiophen-2-yl)ethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3k)

Brown solid, 53 mg, 68% yield, mp 65-67 °C; $R_f = 0.5$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (500 MHz, CDCl_3) δ 8.30 (dd, $J = 8.0, 1.2$ Hz, 1H), 7.82 (dd, $J = 3.8, 1.1$ Hz, 1H), 7.75 – 7.70 (m, 1H), 7.68 (m, 1H), 7.65 (d, $J = 7.6$ Hz, 1H), 7.50 – 7.41 (m, 1H), 7.16 (dd, $J = 4.9, 3.8$ Hz, 1H), 4.41 – 4.31 (m, 1H), 4.08 – 3.99 (m, 1H), 3.91 (dd, $J = 17.4, 3.1$ Hz, 1H), 3.89 – 3.84 (m, 1H), 3.35 – 3.24 (m, 1H), 2.80 – 2.65 (m, 1H), 2.05 – 1.88 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 190.4, 160.9, 160.7, 149.2, 143.7, 134.1, 134.1, 132.4, 128.3, 126.9, 126.5, 126.4, 120.9, 44.9, 41.5, 39.7, 27.1; HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$ 311.0849, Found 311.0852.

3-(2-(Benzo[b]thiophen-2-yl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3l)

Brown solid, 60 mg, 67% yield, mp 81-83 °C; $R_f = 0.6$ (Ethyl Acetate : Hexane = 1:1) ^1H NMR (500 MHz, CDCl_3) δ 8.30 (dd, $J = 8.0, 1.0$ Hz, 1H), 8.08 (s, 1H), 7.89 (t, $J = 8.1$ Hz, 2H), 7.76 – 7.71 (m, 1H), 7.68 (d, $J = 7.9$ Hz, 1H), 7.51 – 7.45 (m, 2H), 7.45 – 7.40 (m, 1H), 4.45 – 4.32 (m, 1H), 4.09 – 3.99 (m, 2H), 3.95 – 3.86 (m, 1H), 3.52 – 3.41 (m, 1H), 2.83 – 2.68 (m, 1H), 2.06 – 1.93 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 191.9, 160.9, 160.7, 142.9, 142.6, 139.1, 134.4, 129.8, 127.8, 126.6, 126.5, 126.1, 125.2, 123.1, 120.7, 45.3, 41.5, 39.8, 26.9; HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{17}\text{N}_2\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$ 361.1005, Found 361.0981.

3-(2-(1H-Indol-2-yl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3m)

Brown solid, 56 mg, 65% yield, mp 170-172 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 9.19 (s, 1H), 8.33 (d, $J = 7.4$ Hz, 1H), 7.81 – 7.65 (m, 3H), 7.52 – 7.43 (m, 2H), 7.42 – 7.36 (m, 1H), 7.33 (s, 1H), 7.23 – 7.16 (m, 1H), 4.45 – 4.34 (m, 1H), 4.05 (dd, $J = 19.5, 8.4$ Hz, 1H), 3.95 (d, $J = 15.8$ Hz, 2H), 3.39 (dd, $J = 16.9, 9.8$ Hz, 1H), 2.71 (s, 1H), 2.09 – 1.96 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 190.1, 161.0, 160.8, 137.4, 134.7, 134.4, 127.5, 126.7, 126.6 (3C), 123.2, 121.2, 120.7, 112.2 (2C), 110.0, 45.2, 40.5, 39.8, 26.9; HRMS (ESI): m/z calcd for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 344.1394, Found 344.1370.

3-(2-((8R,9S,13S,14S)-3-Hydroxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-2-yl)-2-oxoethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3n)

Yellow solid, 74 mg, 60% yield, mp 117-119 °C; $R_f = 0.3$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 11.81 (s, 1H), 8.24 (d, $J = 7.9$ Hz, 3H), 7.77 – 7.55 (m, 1H), 7.51 – 7.33 (m, 1H), 6.68 (s, 1H), 4.34 – 4.23 (m, 1H), 4.05 – 3.93 (m, 1H), 3.92 – 3.77 (m, 2H), 3.35 – 3.24 (m, 1H), 2.91 – 2.81 (m, 2H), 2.71 – 2.62 (m, 1H), 2.50 – 2.41 (m, 2H), 2.40 – 2.34 (m, 1H), 2.18 – 1.83 (m, 10H), 1.23 (d, $J = 9.0$ Hz, 1H), 0.85 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR $\{^1\text{H}\}$ (101 MHz, CDCl_3) δ 196.9, 190.9, 160.7, 160.2, 151.6, 149.2, 147.3, 134.2, 131.3, 126.9, 126.5, 126.4 (3C), 120.8, 117.9, 50.4, 47.9, 44.9, 43.6, 40.6, 39.4, 38.1, 35.9, 31.4,

29.9, 27.2, 26.1, 26.0, 21.6, 13.8; HRMS (ESI): m/z calcd for C₃₁H₃₃N₂O₄ (M+H)⁺ 497.2435, Found 497.2443.

Ethyl-2-(4-isobutoxy-3-(2-(9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl)acetyl)phenyl)-4-methylthiazole-5-carboxylate (3o)

Yellow solid, 90 mg, 66% yield, mp 89-91 °C; R_f = 0.5 (Ethyl Acetate : Hexane = 1:1); ¹H NMR (400 MHz, CDCl₃) δ 8.28 (d, J = 2.4 Hz, 1H), 8.23 (d, J = 7.9 Hz, 1H), 8.04 (dd, J = 8.7, 2.4 Hz, 1H), 7.69 – 7.60 (m, 2H), 7.39 (t, J = 8.0 Hz, 1H), 6.97 (d, J = 8.8 Hz, 1H), 4.36 – 4.31 (m, 1H), 4.30 – 4.24 (m, 3H), 4.06 – 3.98 (m, 2H), 3.87 (d, J = 6.3 Hz, 2H), 2.69 (s, 3H), 2.67 (d, J = 4.4 Hz, 1H), 2.23 – 2.12 (m, 1H), 1.94 – 1.84 (m, 1H), 1.36 – 1.26 (m, 4H), 1.04 (dd, J = 6.7, 3.0 Hz, 6H); ¹³C {¹H}NMR (101 MHz, CDCl₃) δ 198.3, 168.6, 162.3, 161.0, 160.5, 134.3, 132.1, 130.9, 129.4 (2C), 127.6, 126.5 (2C), 126.5, 125.9, 121.5, 121.4, 113.0 (2C), 75.8, 61.3, 46.9, 45.4, 39.9, 28.4, 26.9, 19.6, 19.6, 17.5, 14.4; HRMS (ESI): m/z calcd for C₃₀H₃₂N₃O₅S (M+H)⁺ 546.2057, Found 546.2066.

6-Methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3p)

Yellow solid, 62 mg, 83% yield, mp 159-161 °C ; R_f = 0.5 (Hexane: EtOAc = 1:1); ¹H NMR (400 MHz, CDCl₃) δ 8.19 (d, J = 8.1 Hz, 1H), 8.06 – 8.00 (m, 2H), 7.63 – 7.57 (m, 1H), 7.52 – 7.48 (m, 2H), 7.48 – 7.46 (m, 1H), 7.29 (d, J = 1.3 Hz, 1H), 4.40 – 4.32 (m, 1H), 4.08 – 4.02 (m, 1H), 3.98 (dd, J = 18.1, 3.0 Hz, 1H), 3.94 – 3.84 (m, 1H), 3.37 (s, 1H), 2.81 – 2.68 (m, 1H), 2.49 (s, 3H), 2.00 – 1.86 (m, 1H); ¹³C {¹H}NMR (101 MHz, CDCl₃) δ 197.5, 161.2, 160.9, 149.2, 145.2, 136.5, 133.5, 130.1, 128.8, 128.4, 128.2, 127.9, 126.6, 126.3, 118.4, 44.9, 41.2, 39.6, 27.2, 21.9; HRMS (ESI): m/z calcd for C₂₀H₁₉N₂O₂ (M+H)⁺ 319.1441, Found 319.1445.

6-Methoxy-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3q)

Yellow solid, 56 mg, 77% yield, mp 118-120 °C; R_f = 0.4 (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.19 (d, J = 8.6 Hz, 1H), 8.07 – 7.97 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.02 (dd, J = 11.5, 2.4 Hz, 2H), 4.39 – 4.30 (m, 1H), 4.06 – 4.00 (m, 1H), 3.96 (dd, J = 18.1, 3.1 Hz, 1H), 3.90 (s, 3H), 3.89 – 3.83 (m, 1H), 3.38 – 3.28 (m, 1H), 2.80 – 2.68 (m, 1H), 1.98 – 1.83 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 197.4, 164.4, 161.7, 160.6, 151.5, 136.5, 133.5, 128.8 (2C), 128.2 (2C), 127.9, 116.2, 114.4, 107.8, 55.7, 44.9, 41.1, 39.7, 27.2; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 335.1390, Found 335.1404.

6-(Tert-butyl)-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3r)

Yellow solid; 57 mg, 81% yield, mp 113-115 °C; R_f = 0.5 (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.23 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 7.4 Hz, 2H), 7.66 (d, J = 1.3 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.55 – 7.45 (m, 3H), 4.42 – 4.29 (m, 1H), 4.11 – 3.95 (m, 2H), 3.94 – 3.82 (m, 1H), 3.42 – 3.28 (m, 1H), 2.80 – 2.67 (m, 1H), 2.01 – 1.84 (m, 1H), 1.39 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.4, 161.0, 160.9, 158.2, 149.2, 136.5, 133.5, 130.0, 128.8, 128.4, 128.2, 126.1, 124.5, 123.1, 118.3, 44.9, 41.2, 39.6, 35.4, 31.1, 27.2. HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 361.1911, Found 361.1932.

6-Chloro-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3s)

Yellow solid, 59 mg, 82% yield, mp 134-136 °C; R_f = 0.4 (Ethyl Acetate : Hexane = 1:1); ^1H NMR (500 MHz, CDCl_3) δ 8.22 (d, J = 8.5 Hz, 1H), 8.02 (dd, J = 8.3, 1.2 Hz, 2H), 7.64 (d, J = 2.0 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.52 – 7.48 (m, 2H), 7.41 – 7.38 (m, 1H), 4.42 – 4.31 (m, 1H), 4.07 – 4.00 (m, 1H), 3.98 – 3.92 (m, 1H), 3.92 – 3.84 (m, 1H), 3.35 (m, 1H), 2.80 – 2.70 (m, 1H), 2.01 – 1.89 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.3, 162.4, 160.4, 150.2, 140.2, 136.4, 133.6, 130.0, 128.8, 128.4, 128.1, 127.9, 126.9, 126.5, 119.32, 45.1, 40.9, 39.7, 27.0; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{16}\text{ClN}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 339.0895, Found 339.0900.

6-Bromo-3-(2-oxo-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3t)

Yellow solid, 54 mg, 79% yield, mp 171-173 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1) ^1H NMR (400 MHz, CDCl_3) δ 8.14 (d, $J = 8.5$ Hz, 1H), 8.02 (d, $J = 7.3$ Hz, 2H), 7.83 (d, $J = 1.6$ Hz, 1H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.57 – 7.53 (m, 1H), 7.50 (t, $J = 7.6$ Hz, 2H), 4.41 – 4.31 (m, 1H), 4.08 – 4.00 (m, 1H), 4.00 – 3.91 (m, 1H), 3.90 – 3.83 (m, 1H), 3.40 – 3.32 (m, 1H), 2.82 – 2.70 (m, 1H), 2.01 – 1.87 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.3, 162.3, 160.5, 150.3, 136.4, 133.6, 129.7, 129.6, 128.8 (2C), 128.1 (2C), 127.9 (2C), 119.7, 45.1, 40.9, 39.7, 27.0; HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{16}\text{BrN}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 383.0390, Found 383.0396.

3-(2-Oxo-2-phenylethyl)-6-(trifluoromethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (3u)

White solid, 58 mg, 84% yield, mp 155-157 °C; $R_f = 0.4$ (Ethyl Acetate : Hexane = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.41 (d, $J = 8.3$ Hz, 1H), 8.06 – 8.00 (m, 2H), 7.93 (s, 1H), 7.67 – 7.62 (m, 1H), 7.62 – 7.58 (m, 1H), 7.54 – 7.48 (m, 2H), 4.47 – 4.30 (m, 1H), 4.13 – 4.01 (m, 1H), 3.97 (m, 1H), 3.93 – 3.85 (m, 1H), 3.46 – 3.32 (m, 1H), 2.84 – 2.70 (m, 1H), 2.06 – 1.90 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz, CDCl_3) δ 197.2, 162.6, 160.1, 149.2, 136.4, 135.6 (q, $J = 32.7$ Hz), 133.6, 128.8 (2C), 128.1 (2C), 127.6, 124.5 (q, $J = 3.8$ Hz), 121.3 (d, $J = 272.9$ Hz), 123.2, 122.2 (q, $J = 2.9$ Hz), 45.2, 40.8, 39.7, 26.9; HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 373.1158, Found 373.1176.

3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[g]pyrrolo[2,1-b]quinazolin-11(1H)-one (3v)

Pale yellow, 55 mg, 78% yield, mp 149-151 °C; $R_f = 0.5$ (Ethyl Acetate : Hexane = 1:1) ^1H NMR (400 MHz, CDCl_3) δ 8.90 (d, $J = 8.2$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H), 8.08 (d, $J = 7.5$ Hz, 2H), 7.89 (d, $J = 7.9$ Hz, 1H), 7.80 (d, $J = 8.7$ Hz, 1H), 7.70 – 7.57 (m, 3H), 7.52 (t, $J = 7.5$ Hz, 2H), 4.45 (t, $J = 9.9$ Hz, 1H), 4.17 – 3.99 (m, 3H), 3.44 – 3.30 (m, 1H), 2.90 – 2.68

(m, 1H), 2.06 – 1.91 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.7, 161.1, 161.1, 147.9, 136.7, 136.2, 133.6, 129.9, 129.0, 128.8 (2C), 128.2 (2C), 127.8, 126.6, 126.5, 125.1, 121.7, 117.0, 45.3, 41.1, 40.1, 27.5; HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 355.1441, Found 355.1444.

5-(2-Oxo-2-phenylethyl)-6,7-dihydropyrrolo[1,2-a]thieno[3,2-d]pyrimidin-9(5H)-one (3w)

Brown solid, 61 mg, 81% yield, mp 70-72 °C; R_f = 0.5 (Ethyl Acetate : Hexane = 1:1); ^1H (500 MHz, CDCl_3) δ 8.08 – 7.94 (m, 2H), 7.77 (d, J = 5.2 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.28 (d, J = 5.2 Hz, 1H), 4.48 – 4.36 (m, 1H), 4.13 – 4.03 (m, 1H), 4.00 – 3.87 (m, 2H), 3.46 – 3.32 (m, 1H), 2.84 – 2.73 (m, 1H), 2.06 – 1.90 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.3, 162.9, 158.1, 157.2, 136.4, 134.1, 133.6, 128.8 (2C), 128.1 (2C), 124.6, 121.7, 45.1, 41.2, 39.3, 27.6; HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$ 311.0849, Found 311.0858.

6-methyl-6-(2-oxo-2-phenylethyl)indolo[2,1-b]quinazolin-12(6H)-one (3x)

White solid, 55 mg, 78% yield, mp 135-137 °C; R_f = 0.6 (Hexane:EtOAc = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.69 (d, J = 8.0 Hz, 1H), 8.45 (m, 1H), 7.80 (dd, J = 8.3, 1.1 Hz, 2H), 7.75 – 7.69 (m, 1H), 7.68 – 7.64 (m, 1H), 7.53 – 7.46 (m, 2H), 7.46 – 7.41 (m, 1H), 7.40 – 7.34 (m, 2H), 7.33 – 7.29 (m, 1H), 7.28 – 7.23 (m, 1H), 4.03 (dd, J = 46.6, 18.1 Hz, 2H), 1.68 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 195.6, 164.1, 160.3, 147.6, 139.8, 136.1, 135.9, 134.1, 133.4, 128.6 (2C), 128.5, 127.9 (2C), 127.1, 127.0, 126.5, 126.3, 121.6, 121.5, 117.4, 47.9, 46.2, 27.4; HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 367.1441, Found 367.1456.

6-(2-(4-methoxyphenyl)-2-oxoethyl)-6-methylindolo[2,1-b]quinazolin-12(6H)-one (3y)

Yellow solid, 58 mg, 77% yield, mp 155-157 °C; R_f = 0.4 (Hexane:EtOAc = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 8.71 (d, J = 8.0 Hz, 1H), 8.47 (dd, J = 8.0, 1.0 Hz, 1H), 7.81 (d, J = 8.9 Hz, 2H), 7.77 – 7.72 (m, 1H), 7.69 (d, J = 7.4 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.48 – 7.42 (m,

1H), 7.35 – 7.25 (m, 2H), 6.86 (d, $J = 8.9$ Hz, 2H), 4.00 (dd, $J = 42.3, 17.9$ Hz, 2H), 3.84 (s, 3H), 1.69 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 194.0, 164.2, 163.6, 160.3, 147.7, 139.8, 136.1, 134.0, 130.3 (2C), 129.3, 128.5, 127.1, 127.0, 126.4, 126.2, 121.7, 121.5, 117.3, 113.7 (2C), 55.5, 47.6, 46.3, 27.4; HRMS (ESI): m/z calcd for $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 397.1547, Found 397.1563.

6-(2-(2-hydroxyphenyl)-2-oxoethyl)-6-methylindolo[2,1-b]quinazolin-12(6H)-one (3z)

Yellow solid, 59 mg, 81% yield, mp 159-161 °C; $R_f = 0.4$ (Hexane:EtOAc = 1:1); ^1H NMR (400 MHz, CDCl_3) δ 11.42 (s, 1H), 8.71 (d, $J = 8.0$ Hz, 1H), 8.50 (d, $J = 7.0$ Hz, 1H), 7.83 (d, $J = 6.9$ Hz, 1H), 7.77 (dd, $J = 11.0, 4.1$ Hz, 1H), 7.70 (d, $J = 7.7$ Hz, 1H), 7.54 (t, $J = 7.0$ Hz, 1H), 7.51 – 7.41 (m, 2H), 7.38 – 7.28 (m, 2H), 6.97 – 6.84 (m, 2H), 4.09 (dd, $J = 44.9, 18.2$ Hz, 2H), 1.70 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 163.8, 162.2, 160.3, 147.5, 139.7, 136.6, 135.6, 134.2, 129.5, 128.7, 127.1, 127.0, 126.6, 126.3, 121.6, 121.5, 118.9 (2C), 118.6, 117.4, 47.4, 45.9, 27.4; HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{19}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 383.1390, Found 383.1407.

Gram scale synthesis of (3a):

N-Cyano benzamide (5 mmol, 1 equiv), aryl aldehyde (10 mmol, 2 equiv), and di-*tert*-butyl peroxide (25 mmol, 5 equiv) were taken in a seal tube, and 15 mL of fluorobenzene was added. The reaction mixture was stirred at 130 °C (oil bath temperature) for 20 h. After completion of the reaction (monitored by TLC), the reaction mass was extracted with ethyl acetate (20 mL \times 3). The combined organic layers were dried over Na_2SO_4 and concentrated, and the crude reaction mixture was purified by column chromatography on silica gel using ethyl acetate and hexanes as an eluent to afford the desired product 3a in 78% yield.

3-(2-Hydroxy-2-phenylethyl)-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one (4)

Compound 3a (50 mg, 0.16 mmol) was taken in a 10 mL round-bottom flask, dissolved in methanol (3 mL) under a N_2 atmosphere. Then, NaBH_4 (9 mg, 0.24 mmol) was added into the

reaction mixture and stirred at room temperature for 2 h. After completion of reaction (indicated by TLC), the reaction mixture was quenched by NH₄Cl solution and methanol was evaporated under reduced pressure. The residual fraction was extracted with ethyl acetate, and concentrated. The residue was purified by column chromatography to obtain **4** as a brown solid, 61 mg, 80% yield, mp 110-112 °C; R_f = 0.3 (Hexane : Ethyl Acetate = 1:1); ¹H NMR (400 MHz, CDCl₃) δ 8.28 (m, 1H(both isomer)), 7.80 – 7.69 (m, 2H(both isomer)), 7.53 – 7.42 (m, 3H (both isomer)), 7.41 – 7.33 (m, 2H (both isomer)), 7.31 – 7.24 (m, 1H (both isomer)), 5.23 – 5.00 (m, 1H (both isomer)), 4.44 – 4.25 (m, 1H (both isomer)), 4.01 – 3.81 (m, 1H (both isomer)), 3.69 – 3.11 (m, 1H (both isomer)), 2.62 – 2.46 (m, 1H (both isomer)), 2.39 – 2.22 (m, 1H (both isomer)), 2.18 – 1.88 (m, 2H both isomer)). ¹³C{¹H}NMR (101 MHz, CDCl₃) δ 162.2, 162.1, 160.6, 160.5, 147.6, 147.5, 145.1, 144.2, 134.5 (2C), 128.5 (3C), 127.4 (2C), 127.1, 126.8 (2C), 126.5, 126.4 (2C), 126.3, 125.8 (2C), 125.6 (2C), 120.4, 120.3, 74.1, 71.7, 45.3, 45.2, 44.2, 42.7, 40.6, 40.4, 27.9, 27.8; HRMS (ESI): m/z calcd for C₁₉H₁₈N₂O₂ (M+H)⁺ 307.1441, Found 307.1452.

(Z)-3-(2-(Methoxyimino)-2-phenylethyl)-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1H)-one (**5**)

To a stirring solution of compound **3a** (50 mg, 0.16 mmol) in 3 mL of pyridine was added O-benzylhydroxylamine hydrochloride salt (21 mg, 0.24 mmol) in one portion. After 17 h the solvent was removed in vacuo, then the residue was extracted with ethyl acetate, and concentrated. The residue was purified by column chromatography to obtain **5** as a brown solid, 65 mg, 78% yield, mp 77-79 °C; R_f = 0.4 (Hexane : Ethyl Acetate = 1:1); ¹H NMR (500 MHz, CDCl₃) δ 8.18 (d, *J* = 7.7 Hz, 1H), 7.66 – 7.60 (m, 4H), 7.41 – 7.33 (m, 1H), 7.30 – 7.24 (m, 3H), 4.17 – 4.10 (m, 1H), 3.90 (s, 3H), 3.89 – 3.82 (m, 1H), 3.53 – 3.45 (m, 1H), 3.39 (m, 1H), 3.21 (dd, *J* = 13.4, 10.5 Hz, 1H), 2.22 – 2.13 (m, 1H), 1.96 – 1.86 (m, 1H). ¹³C{¹H}NMR (101 MHz, CDCl₃) δ 160.9, 160.7, 155.8, 148.9, 134.9, 134.2, 129.5, 128.7

(2C), 126.9, 126.5 (2C), 126.4, 120.7, 62.1, 44.8, 41.5, 28.2, 26.1; HRMS (ESI): m/z calcd for C₂₀H₁₉N₃O₂ (M+H)⁺ 334.1551, Found 334.1558.

ASSOCIATED CONTENT:

• Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

¹H and ¹³C and ¹⁹F NMR spectra copies of all the new compounds.

ACKNOWLEDGEMENTS

The authors thank Indo-French Centre for the Promotion of Advanced Research, New Delhi for funding the project (No.6505-3). U.A. thanks the Department of Science and Technology for research fellowship (DST-INSPIRE Award No. IF180803). [CSIR-IICT Communication no. IICT/Pubs./ 2024/069.]

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