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Eco-friendly reactions in PEG-400: a highly efficient and green approach for stereoselective access to multisubstituted 3,4-dihydro-2(1*H*)-quinazolines using 2-aminobenzylamines†

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An efficient and stereoselective synthesis of novel 3,4-dihydro-2(1*H*)-quinazolines has been developed through cyclization reactions of 2-aminobenzylamines with α -oxoketene dithioacetals using PEG-400 as an inexpensive, easy to handle, non-toxic and recyclable reaction medium. The developed protocol is operationally simple and tolerates various substrates having different functionalities. This protocol features several attributes such as excellent yields, no work up, green reaction conditions, and being environmentally benign. The attractive feature of this new strategy is that all the reported final compounds have been isolated as single (*E*)-stereoisomeric forms, which was confirmed by ¹HNMR and X-ray crystallographic studies.

Introduction

Quinazolines are a class of fused heterocyclic ring systems containing multiple pharmacophores which are undoubtedly well established as biologically and pharmaceutically important compounds.¹ Quinazoline-based heterocycles and their hydrated congeners have been reported to possess diverse biological and therapeutic properties such as inhibition of the epidermal growth factor (EGF) receptors of tyrosine kinase,^{2a} and analgesic,^{2b-d} anticancer,³ anti-inflammatory,⁴ antidiuretic,⁵ anticonvulsant⁶ and anti-Alzheimer⁷ activities. Commercialized drug compounds such as gefitinib (I), erlotinib (II), alfuzosin (III), and afloqualone (IV) are some notable examples of drugs containing quinazoline as a core nucleus (Fig. 1). Considering these applications, development of novel synthetic routes towards the formation of these pharmaceutically important scaffolds attracts the interest of synthetic organic chemists.

Substituted quinazolines have been reported to be constructed by numerous methods involving several substrates.⁸⁻¹⁰ Among them, many of the synthetic methodologies have craftily employed 2-aminobenzylamines as substrates with aldehydes for the synthesis of quinazolines (Scheme 1, i-iv). These reactions have been carried out by using (i) [Cp*IrCl₂]₂ as a catalyst, four equivalents of styrene in xylene solvent under inert atmosphere of N₂, 24 h, reflux conditions^{11a} (Scheme 1, a); (ii)

nanoclusters of bi-metallic Pt/Ir alloy as a catalyst, 5,5',6,6'-tetrahydroxy-3,3',3'-tetramethyl-1,1'-spiro-bisindane, (TTSBI) as a co-catalyst, K₂CO₃ as a base with CDCl₃/H₂O as solvent for a longer reaction duration^{11b} (Scheme 1, b); (iii) a CuCl/DABCO/4-HO-TEMPO/O₂ catalytic system in CH₃CN at 80 °C (ref. 12a) (Scheme 1, c) and (iv) four equivalents of NaOCl as oxidant in MeOH solvent for longer reaction hours^{12b} (Scheme 1, d). However, despite the synthetic utility of these protocols, the reported techniques suffer from drawbacks such as the use of expensive metal catalyst along with a co catalyst and requirement of a stoichiometric amount of toxic oxidant NaOCl for the transformation to take place. In such a scenario, development of a catalyst free and eco friendly methodology to deliver functionalized quinazolines will provide an intriguing and green alternative to the conventional approach.

Over the years, there has been a growing public concern towards the adverse effects of toxic and volatile organic solvents

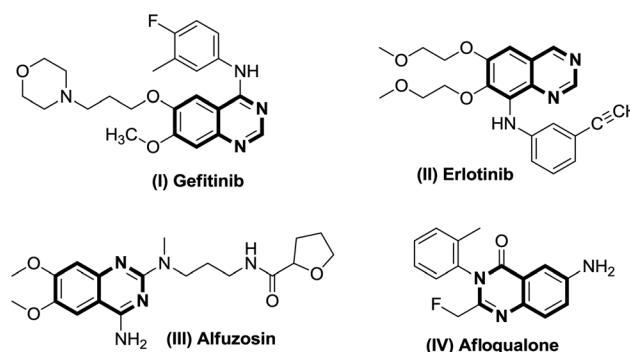


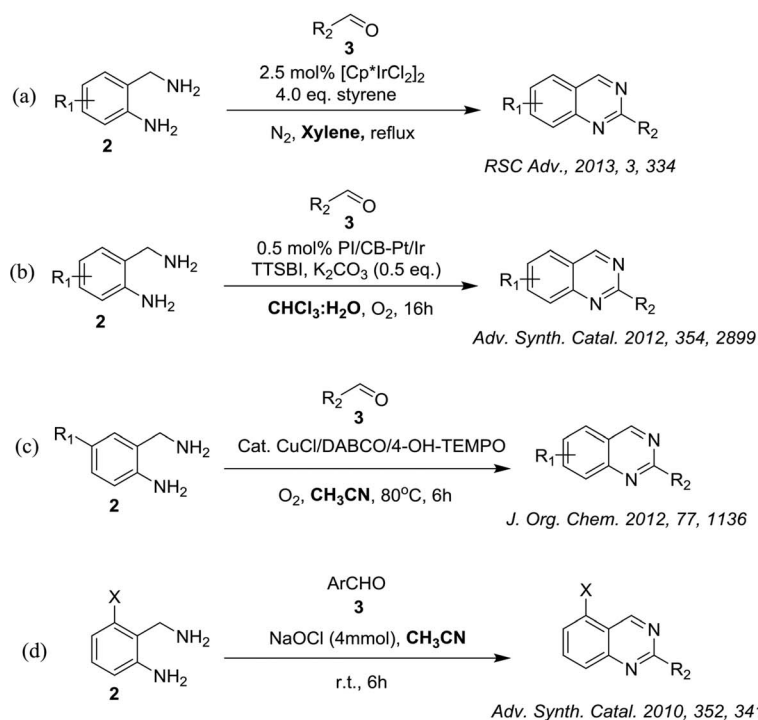
Fig. 1 Some popular marketed drugs containing quinazoline as a core nucleus.

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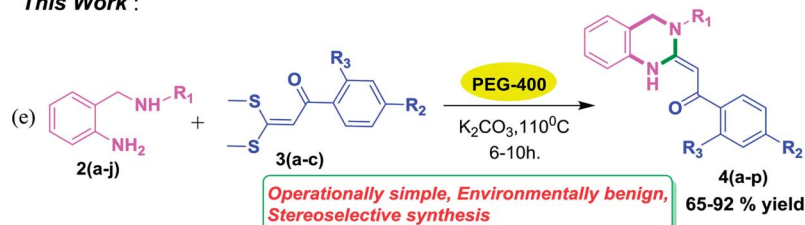
† Electronic supplementary information (ESI) available: Datas and spectral copies of ¹H, ¹³C NMR for target compounds. X-ray crystallographic data of compound **4o** with CCDC No. 1055453. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra13487h



i. Previous synthetic approaches



This Work :



R_1 = H, methyl, ethyl, n-propyl, isopropyl, n-butyl, tert.-butyl, cyclopropyl, cyclohexyl, benzyl
 R_2 = F, CF₃
 R_3 = OCH₃


Scheme 1 Previous synthetic approaches and our designed approach.

and the search for alternate nonhazardous reaction media is gaining progress. Meanwhile, using water as a green solvent has been well documented¹³ but its practical use is limited due to the hydrophobic nature of organic compounds.¹⁴ On the contrary, PEGs have been explored as powerful, novel, eco-friendly reaction media for innumerable organic transformations¹⁵ owing to their non toxic, inexpensive, thermally stable, readily recyclable, and biodegradable nature.¹⁶ In continuation of our research studies aimed at developing environmentally benign and improved synthetic methodologies for organic reactions,¹⁷ we herein report for the first time an efficient and green approach for the stereoselective synthesis of 3,4-dihydro-2(1H)-quinazolines *via* substituted 2-amino benzylamines and α -oxoketene dithioacetals as building blocks using PEG-400 as an eco-friendly reaction medium (Scheme 1, e). To the best of our knowledge, there have been no reports on the synthesis of 3,4-dihydro-2(1H)-quinazolines using PEG-400 as a solvent under catalyst-free conditions.

Results and discussion

To check feasibility of this route, a model reaction between **2b** and **3a** was performed by varying different protic and aprotic solvents and various bases (Table 1). When the reaction was performed using EtOH as polar protic solvent and CH₃CN as low boiling aprotic solvent under reflux conditions using K₂CO₃ as base, the desired product **4b** was obtained in lower yields (Table 1, entries 1 and 2). Whereas under similar conditions, high boiling aprotic solvent such as toluene was not proven very effective and gave the desired product **4b** in 50% yield after 12 h (Table 1, entry 3). High boiling polar aprotic solvents like DMF and DMSO afforded the desired product in higher yield taking less time (Table 1, entries 4 and 5). It should be noted that use of polar protic solvents like *n*-BuOH and *t*-BuOH increased the yield to 65% and 70% in the presence of K₂CO₃ as base in 10 h (Table 1, entries 6 and 7). Keeping in view the economical and environmental concerns, H₂O was screened as the reaction



Table 1 Optimization of reaction conditions^a


Entry	Solvent	Base	Temp (°C)	Time (h)	Yield ^b (%)
1	EtOH	K ₂ CO ₃	80	15	40
2	CH ₃ CN	K ₂ CO ₃	90	18	45
3	Toluene	K ₂ CO ₃	110	12	50
4	DMF	K ₂ CO ₃	120	10	60
5	DMSO	K ₂ CO ₃	120	10	62
6	<i>n</i> -BuOH	K ₂ CO ₃	120	10	65
7	<i>t</i> -BuOH	K ₂ CO ₃	85	10	70
8	H ₂ O	K ₂ CO ₃	100	15	Trace
9	PEG 400	K ₂ CO ₃	110	8	90
10	PEG 400 : H ₂ O	K ₂ CO ₃	110	8	81
11	PEG 400 : EtOH	K ₂ CO ₃	110	10	72
12	PEG 400	K ₂ CO ₃	120	8	90
13	PEG 400	K ₂ CO ₃	90	8	80
14	PEG 400	Na ₂ CO ₃	110	8	85
15	PEG 400	TEA	110	8	65
16	PEG 400	DIPEA	110	8	68
17	PEG 400	—	110	8	20

^a Reactions were performed using 1 equiv. of 3a, 1.2 equiv. of 2b, 3.0 equiv. of base. ^b Isolated yield.

medium but observations indicated trace amount of product formation due to solubility problem (Table 1, entry 8). In order to improve the efficiency of the reaction, we next performed our model reaction in PEG-400 at 110 °C using K₂CO₃ as base, and to our delight corresponding product 4b was obtained in a maximum yield of 90% within 8 h (Table 1, entry 9). Encouraged by the above result, a mixture of PEG-400 and H₂O (1 : 1), was used as reaction medium which resulted in the formation of product 4b in 81% yield (Table 1, entry 10). Moreover, change of combination of solvents from PEG-400 and H₂O to PEG-400 and EtOH (1 : 1) also had a detrimental effect on the yield of the product (Table 1, entry 11). Further increase or decrease in the temperature of the reaction could not increase the yield of the desired product 4b (Table 1, entries 12 and 13). From Table 1, it is clear that PEG-400 unanimously dominates as effective solvent medium because it increases the solubility of reactants, which leads to larger interfacial area and lower mass transfer resistance.¹⁸ When base was changed from K₂CO₃ to Na₂CO₃ at 110 °C, 85% yield was observed in 8 h (Table 1, entry 14).

Screening of other organic bases such as TEA and DIPEA in same reaction conditions resulted in 65% and 68% yields respectively (Table 1, entries 15 and 16). However the yield of reaction was drastically reduced to 20% when the reaction was performed in the absence of base (Table 1, entry 17). These optimization studies led to the conclusion that PEG-400 with K₂CO₃ is the reaction medium of choice for this transformation. The reaction product was fully characterized by the IR, ¹H NMR,

¹³C NMR & HRMS data. Compound 4b existed in one stereoisomeric form (*E*-form) as evident from its IR & ¹H NMR data. IR spectra strongly indicated a hydrogen-bonded carbonyl stretching vibration, which was merged with bands around and below 1600 cm⁻¹ (1594 cm⁻¹ in this case). The signals for vinylic proton appeared as sharp singlets, indicating the purity of the geometrical isomers. ¹H NMR spectrum showed a characteristic chelated -NH proton far downfield at δ 13.66, assigned to the amino group which participated in a strong hydrogen bond with oxygen of the carbonyl group in a six membered, planar chelate¹⁹ (Fig. 2). Moreover, ¹H NMR analysis of crude reaction mixture of 4g (see ESI,† page 31) also indicated the formation of one stereoisomeric form of the product. Its spectral data analysis confirmed the structure.

In the ¹H NMR spectrum, presence of peaks as sharp singlets at δ 5.43 (s, 1H) and δ 4.45 (s, 2H), were characterized for vinylic proton and methylene group -NCH₂- in 4b. In the ¹³C NMR spectrum of 4b, characteristic peak at δ 75.9 and δ 50.7 was observed for vinylic carbon and methylene carbon. HRMS data of the compound showed M + 1 peak. Similarly all other compounds were also characterized by IR, ¹H NMR, ¹³C NMR and HRMS studies. The structure of the product 4o was determined by single crystal X-ray diffraction (Fig. 3). The structures of the other products were concluded by analogy.

With these optimized conditions in hand, the scope and robustness of the protocol was explored by employing diversely substituted 2-amino benzylamines 2a-j with α -oxoketene dithioacetals 3a-c (Table 2). We observed that amines 2a-g having aliphatic substitution such as methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl and *tert*-butyl at R¹ afforded the desired stereoselective products 4a-g, 4l & 4n in good to excellent yields of 80–92% with α -oxoketene dithioacetals 3a-c (Table 2, entries 1–7, 12, 14). However, the same α -oxoketene dithioacetals 3a-c provided the products 4h-k, 4m & 4o-p in comparatively lower yields of 65–71% when amines 2h-j bearing aromatic and cyclic

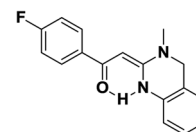


Fig. 2 Stereoselectivity via formation of six membered planar chelate.

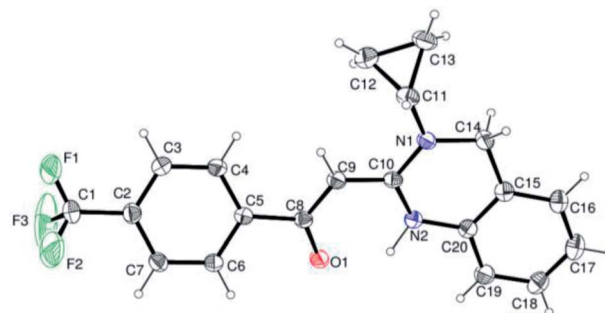


Fig. 3 Ortep diagram of compound 4o.



Table 2 Substrate scope of substituted 3,4-dihydro-2(1*H*)-quinazolines^a

Entry	Substrate (2)	Amine (3)	Product (4)	Yield ^b (%)
1				80
2		3a		90
3		3a		88
4		3a		85
5		3a		82
6		3a		92
7		3a		86

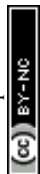


Table 2 (Contd.)

Entry	Substrate (2)	Amine (3)	Product (4)	Yield ^b (%)
8		3a		70
9		3a		71
10		3a		68
11	2i			65
12	2f	3b		82
13	2h	3b		70



Table 2 (Contd.)

Entry	Substrate (2)	Amine (3)	Product (4)	Yield ^b (%)
14	2f	3c	4n	80
15	2h	3c	4o	65
16	2i	3c	4p	66

^a Unless otherwise specified, reactions were performed using 1 equiv. of **3a**, 1.2 equiv. of **2b**, 3.0 equiv. of base. ^b Isolated yield.

groups such as benzyl, cyclopropyl and cyclohexyl at **R**¹ were used (Table 2, entries 8–11, 13, 15–16). This can be attributed to the lesser reactivity of aromatic and cyclic amines due to the involvement of lone pair of $-NH_2$ in conjugation in the former and attachment of $-NH_2$ group to a sp^2 hybridized carbon atom in the later as compared to aliphatic amines.

In order to justify sustainable chemistry issues, recovery and reusability of PEG-400 was studied using the reaction of **2g** & **3a** in the presence of PEG-400 (10 ml) at 110 °C for 6–10 h. After the completion of reaction, reaction mass was then cooled and solvent was evaporated under vacuum. Since PEG is immiscible with diethyl ether, it was washed (two times) with this solvent to remove any unwanted organic impurities and was used successfully in consecutive runs (the yield decreased from 86% to 72% after 5 runs, Table 3), although a weight loss of

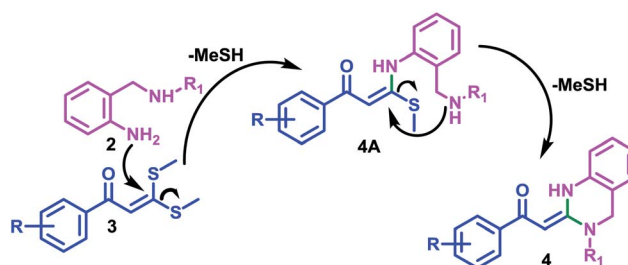
Table 3 Recycling of PEG-400

Runs	1	2	3	4	5
Yield (%)	86	84	80	76	72

approximately 5% of PEG was observed from cycle to cycle due to mechanical loss.

A plausible mechanism for the 3,4-dihydro-2(1H)-quinazolinone ring formation is depicted in Scheme 2. The mechanism first involves the substitution of the thiomethyl group of α -oxoketene dithioacetal **3** by that amino group of reactant **2** which is directly attached to aromatic ring, resulting in the formation of intermediate **4A** at first.

This can be assigned to the presence of characteristic chelated proton of $-NH$ at very high chemical shift values (δ 14–



Scheme 2 Plausible Mechanism.



15 ppm) in the ^1H NMR data of compounds **4(a-p)**. After that, second thiomethyl group is replaced by second amino group of reactant **2** resulting in formation of cyclized product **4** with subsequent elimination of $-\text{MeSH}$.

Conclusions

In conclusion, we have succeeded in developing first novel, inexpensive, cleaner and green methodology for the synthesis of 3,4-dihydro-2(1*H*)-quinazolines. Moreover, avoid of work-up make this new strategy attractive, easy to execute and facile for the assembly of a wide variety of biologically relevant dihydroquinazolines. As the methodology is completely devoid of anhydrous solvents or any catalysts, this approach therefore exemplifies the reconciliation of operational simplicity and economic viability in an environmental friendly time and cost effective manner. It is noteworthy that α -oxoketene dithioacetals and substituted 2-amino benzylamines selectively afforded a single isomer. Further applicability of PEG-400 as solvent system to a wide range of substrates towards the development of catalyst free pathways for synthesizing diverse range of biologically important heterocycles is an ongoing goal of research in our laboratory.

Experimental

General information and method

All the reactions were performed in an oven-dried Schlenk flask under nitrogen atmosphere. Column chromatography was performed using silica gel (mesh 100–200). TLC analysis was performed on commercially prepared 60 F254 silica gel plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining over I_2 chamber. IR spectra was recorded in CHCl_3 on a Perkin Elmer Spectrum RX-1 FT-IR spectrophotometer. CDCl_3 was used as NMR solvent for characterization of compounds. The ^1H NMR spectra were recorded on a Jeol JNM-ECX400P at 400 MHz. The ^{13}C NMR spectra on Jeol JNM-ECX400P at 100 MHz. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, br s = broad singlet), coupling constants in Hertz, and integration. HRMS (ESI) were recorded with Q-TOF electrospray mass spectrometer. All purchased chemicals were used as received. All melting points are uncorrected.

General procedure for synthesis of 2-*N*-aryl/alkyl substituted anilines (**2a-j**)

Compounds **2a-j** were synthesized by reductive amination²⁰ of 2-nitro benzaldehyde with various aliphatic, aromatic and cyclic amines followed by reduction²¹ of nitro group using 10% Pd-C/ H_2 in EtOH at 50 Psi for 2–3 h. Formation of compounds **2a-j** was confirmed by ^1H NMR, ^{13}C NMR and HRMS data.

Analytical data of 2-amino benzylamines

2-(aminomethyl)aniline (2a). The compound was obtained as a light brown solid, yield: 80%; ^1H NMR (400 MHz, DMSO-d_6) δ : 7.03 (dd, $J = 7.33, 1.37$ Hz, 1H), 6.94 (td, $J = 7.79, 1.37$ Hz, 1H), 6.60 (dd, $J = 7.79, 0.92$ Hz, 1H), 6.50 (td, $J = 7.33, 0.92$ Hz, 1H), 4.98 (t, $J = 5.50$ Hz, 2H, $-\text{CH}_2\text{NH}_2-$), 4.88 (bs, 2H, $-\text{NH}_2$), 4.36 (s, 2H, $-\text{CH}_2\text{NH}_2-$); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 146.3, 127.7, 127.6, 125.3, 115.8, 114.5, 61.2 (benzylic- CH_2-); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_7\text{H}_{10}\text{N}_2$: 123.0922, found 123.0913.

2-((methylamino)methyl)aniline (2b). The compound was obtained as a dark green solid, yield: 85%; ^1H NMR (400 MHz, DMSO-d_6) δ : 7.20 (dd, $J = 7.33, 1.37$ Hz, 1H), 7.05 (td, $J = 7.33, 1.37$ Hz, 1H), 6.70 (dd, $J = 8.24, 1.37$ Hz, 1H), 6.54 (td, $J = 7.33, 1.37$ Hz, 1H), 3.96 (s, 2H, benzylic- CH_2-), 2.49 (s, 3H, $-\text{NHCH}_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 147.7, 132.0, 129.8, 116.1, 115.8, 115.2, 47.5 (benzylic- CH_2-), 32.0 ($-\text{NHCH}_3$); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_8\text{H}_{12}\text{N}_2$: 137.1078, found 137.1073.

2-((ethylamino)methyl)aniline (2c). The compound was obtained as a dark green solid, yield: 83%; ^1H NMR (400 MHz, DMSO-d_6) δ : 7.16 (d, $J = 7.79$ Hz, 1H), 7.02 (t, $J = 8.24$ Hz, 1H), 6.68 (d, $J = 7.79$ Hz, 1H), 6.55 (t, $J = 7.33$ Hz, 1H), 5.69 (bs, 2H, $-\text{NH}_2$), 3.86 (s, 2H, benzylic- CH_2-), 2.81 (q, $J = 7.33$ Hz, 2H, $-\text{CH}_2\text{CH}_3$), 1.16 (t, $J = 7.33$ Hz, 3H, $-\text{CH}_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 147.6, 131.0, 129.5, 128.8, 117.4, 115.4, 47.2 (benzylic- CH_2-), 42.1 ($-\text{CH}_2\text{CH}_3$), 11.9 ($-\text{CH}_3$); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_9\text{H}_{14}\text{N}_2$: 151.1235, found 151.1228.

2-((propylamino)methyl)aniline (2d). The compound was obtained as a dark green solid, yield: 80%; ^1H NMR (400 MHz, DMSO-d_6) δ : 7.21 (d, $J = 7.79$ Hz, 1H), 7.01 (t, $J = 8.24$ Hz, 1H), 6.68 (d, $J = 8.24$ Hz, 1H), 6.53 (t, $J = 7.33$ Hz, 1H), 3.94 (s, 2H, benzylic- CH_2-), 2.79 (t, 2H, $J = 7.79$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_3$), 1.65 (sext, 2H, $J = 7.79$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_3$), 0.84 (t, 3H, $J = 7.33$ Hz, $-\text{CH}_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 147.4, 132.7, 131.8, 119.5, 118.1, 116.9, 49.8 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 47.8 (benzylic- CH_2-), 20.1 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 11.9 ($-\text{CH}_3$); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_{10}\text{H}_{16}\text{N}_2$: 165.1391, found 165.1379.

2-((isopropylamino)methyl)aniline (2e). The compound was obtained as dark green solid, yield: 81%; ^1H NMR (400 MHz, CDCl_3) δ : 7.16 (d, $J = 7.79$ Hz, 1H), 7.02 (t, $J = 8.24$ Hz, 1H), 6.68 (d, $J = 7.79$ Hz, 1H), 6.55 (t, $J = 7.33$ Hz, 1H), 3.92 (s, 2H, benzylic- CH_2-), 4.29–4.23 (m, 1H, $-\text{NHCH}$), 1.25 (s, 6H, 2 \times CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 147.6, 131.0, 129.5, 128.8, 117.4, 115.4, 50.9 ($-\text{NHCH}$), 46.5 (benzylic- CH_2-), 23.6 ($-\text{CH}_3$); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_{10}\text{H}_{16}\text{N}_2$: 165.1391, found 165.1358.

2-((butylamino)methyl)aniline (2f). The compound was obtained as a green solid, yield: 86%; ^1H NMR (400 MHz, DMSO-d_6) δ : 7.21 (dd, $J = 7.32, 1.46$ Hz, 1H), 7.07 (dt, $J = 8.05, 1.46$ Hz, 1H), 6.70 (dd, $J = 8.05, 1.46$ Hz, 1H), 6.57 (t, $J = 7.32, 1.46$ Hz, 1H), 3.97 (s, 2H, benzylic- CH_2-), 2.87 (t, 2H, $J = 8.05$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2$), 1.62 (q, 2H, $J = 8.05$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2$), 1.30 (sext, 2H, $J = 7.32$ Hz, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 0.87 (t, 3H, $J = 7.69$ Hz, $-\text{CH}_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ : 147.6, 132.1, 129.8, 116.2, 115.9, 115.2, 46.2 (benzylic- CH_2-), 38.4 ($-\text{NCH}_2$), 27.3 ($-\text{CH}_2\text{CH}_2\text{CH}_2$), 19.4 ($-\text{CH}_2\text{CH}_3$), 13.5 ($-\text{CH}_3$); HRMS (ESI) ($\text{M} + \text{H}$)⁺ calcd for $\text{C}_{11}\text{H}_{18}\text{N}_2$: 179.1548, found 179.1537.



2-((tert-butylamino)methyl)aniline (2g). The compound was obtained as a dark green solid, yield: 87%; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 7.00 (d, $J = 7.33$ Hz, 1H), 6.93 (t, $J = 7.79$ Hz, 1H), 6.60 (d, $J = 7.79$ Hz, 1H), 6.48 (t, $J = 7.33$ Hz, 1H), 3.62 (s, 2H, benzylic- CH_2 -), 1.14 (s, 9H, 3 \times CH_3); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6) δ : 147.5, 130.0, 127.5, 116.6, 115.3, 114.3, 51.5 (-NHC), 42.5 (benzylic- CH_2 -), 27.6 (- CH_3); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{11}\text{H}_{18}\text{N}_2$: 179.1548, found 179.1540.

2-((cyclopropylamino)methyl)aniline (2h). The compound was obtained as a light green solid, yield: 87%; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 6.97 (d, $J = 7.32$ Hz, 1H), 6.92 (t, $J = 7.93$, 7.32 Hz, 1H), 6.58 (d, $J = 7.32$ Hz, 1H), 6.47 (t, $J = 7.32$ Hz, 1H), 3.63 (s, 2H, benzylic- CH_2 -), 2.06–2.03 (m, 1H, -NHCH), 0.36–0.31 (m, 2H, cyclopropyl CH_2), 0.25–0.22 (m, 2H, cyclopropyl CH_2); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6) δ : 147.2, 129.1, 127.4, 123.6, 115.8, 114.6, 51.2 (benzylic- CH_2 -), 30.2 (-NHCH), 5.8 (cyclopropyl CH_2).

2-((cyclohexylamino)methyl)aniline (2i). The compound was obtained as a dark green liquid, yield: 84%; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 7.21 (dd, $J = 7.32$, 1.46 Hz, 1H), 7.06 (t, $J = 8.05$ Hz, 1H), 6.70 (d, $J = 8.05$ Hz, 1H), 6.57 (t, $J = 7.32$ Hz, 1H), 3.96 (s, 2H, benzylic- CH_2 -), 2.99–2.94 (m, 1H, -NCH), 2.13–2.10 (d, 2H), 1.77–1.74 (d, 2H), 1.60–1.57 (d, 1H), 1.42–1.33 (m, 2H), 1.25–1.06 (m, 3H); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6) δ : 147.4, 131.8, 130.6, 117.6, 116.8, 57.3 (-NHCH), 31.2, 25.2, 24.6.

2-((benzylamino)methyl)aniline (2j). The compound was obtained as a light green solid, yield: 82%; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 7.59 (d, $J = 7.32$ Hz, 1H), 7.50 (d, $J = 7.32$ Hz, 1H), 7.41–7.34 (m, 3H), 7.22 (d, $J = 7.32$ Hz, 1H), 7.06 (t, $J = 7.32$ Hz, 1H), 6.72 (d, $J = 7.32$ Hz, 1H), 6.68 (d, $J = 7.32$ Hz, 1H) 4.14 (s, 2H, benzylic- CH_{2a} -), 4.00 (s, 2H, benzylic- CH_{2b} -); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 146.9, 140.2, 129.8, 128.5, 127.5, 127.3, 127.1, 124.2, 118.5, 116.3, 56.8 (benzylic- CH_{2a} -), 48.9 (benzylic- CH_{2b} -); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2$: 213.1391, found 213.1387.

General procedure for the synthesis 3,4-dihydro-1H-quinazolin-2-ylidenes (4a–p)

In an oven-dried two-neck RBF, α -oxoketene dithioacetal **3a–c** (1 equiv.), 1.2 equiv. of 2-substituted aniline **2a–j**, 3.0 equiv. of K_2CO_3 was added in 10 mL of PEG-400. Reaction mass was heated at 110 $^\circ\text{C}$ for 6–10 h. Progress of reaction was monitored by TLC. The reaction mixture was then cooled and solvent was evaporated under vacuum. Crude was directly purified by column chromatography using silica gel (100 : 200 mesh) in 5–10% ethyl acetate/hexane as eluent to afford the corresponding product. Since PEG is immiscible with diethyl ether, it was washed (two times) with this solvent to remove any unwanted organic impurities and was used successfully in consecutive runs. Although a weight loss of approximately 5% of PEG was observed from cycle to cycle due to mechanical loss.

Analytical data of 3,4-dihydro-1H-quinazolin-2-ylidenes

(E)-2-(3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4a). The compound was obtained as light yellow solid, yield: 80%; mp 104–106 $^\circ\text{C}$; IR (ν_{max} cm^{-1}) (CHCl_3): 2923,

2358, 1589; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ : 13.23 (bs, 1H, NH), 7.90 (dd, $J = 9.0$, 3.3 Hz, 2H), 7.34–7.27 (m, 1H), 7.14–7.06 (m, 4H), 7.00 (d, $J = 7.8$ Hz, 1H), 5.68 (s, 1H, vinylic CH), 5.19 (s, 2H, -NHCH $_2$); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 187.2 (C=O), 165.8, 164.2, 135.7, 132.8, 129.5, 129.0, 124.5, 123.8, 119.3, 115.3, 115.1, 79.1 (vinylic CH), 45.7 (-NHCH $_2$); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{16}\text{H}_{13}\text{FN}_2\text{O}$: 269.1090, found 269.1085.

(E)-1-(4-fluorophenyl)-2-(3-methyl-3,4-dihydroquinazolin-2(1H)-ylidene)ethanone (4b). The compound was obtained as a yellow solid, yield: 90%; mp 138–140 $^\circ\text{C}$; IR (ν_{max} cm^{-1}) (CHCl_3): 2923, 1594; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 13.66 (s, 1H, NH), 7.92 (dd, $J = 9.16$, 3.05 Hz, 2H), 7.18 (t, $J = 9.16$ Hz, 3H), 7.07 (d, $J = 6.71$ Hz, 1H), 6.96 (t, $J = 7.32$ Hz, 1H), 6.91 (d, $J = 7.93$ Hz, 1H), 5.43 (s, 1H, vinylic CH), 4.45 (s, 2H, -NCH $_2$), 3.03 (s, 3H, - CH_3); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 184.1 (C=O), 165.2, 162.7, 157.4, 137.5, 134.2, 128.6, 125.4, 122.8, 117.9, 115.3, 115.0, 114.8, 75.9 (vinylic CH), 50.7 (-NCH $_2$), 37.5 (- CH_3); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{17}\text{H}_{15}\text{FN}_2\text{O}$: 283.1246, found 283.1245.

(E)-2-(3-ethyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4c). The compound was obtained as yellow solid, yield: 88%; mp 84–86 $^\circ\text{C}$; IR (ν_{max} cm^{-1}) (CHCl_3): 2925, 1593; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 13.86 (s, 1H, NH), 7.93 (dd, $J = 9.16$, 3.05 Hz, 2H), 7.21 (t, $J = 8.85$ Hz, 3H), 7.11 (d, $J = 7.32$ Hz, 1H), 6.99 (t, $J = 7.32$ Hz, 1H), 6.93 (d, $J = 7.93$ Hz, 1H), 5.50 (s, 1H, vinylic CH), 4.49 (s, 2H, -NCH $_2$), 3.51 (q, 2H, - CH_2CH_3), 1.21 (t, 3H, - CH_3); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 183.9 (C=O), 165.1, 162.6, 156.7, 137.7, 134.3, 128.6, 128.5, 125.4, 122.8, 117.9, 115.2, 114.9, 114.7, 75.7 (vinylic CH), 48.1 (-NCH $_2$), 45.0 (- CH_2CH_3), 11.2 (- CH_3); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_2\text{O}$: 297.1403, found 297.1396.

(E)-1-(4-fluorophenyl)-2-(3-propyl-3,4-dihydroquinazolin-2(1H)-ylidene)ethanone (4d). The compound was obtained as light yellow solid, yield: 85%; mp 130–132 $^\circ\text{C}$; IR (ν_{max} cm^{-1}) (CHCl_3): 2924, 1590; $^1\text{H NMR}$ (300 MHz, DMSO- d_6) δ : 13.91 (s, 1H, NH), 7.93 (dd, $J = 8.70$, 3.6 Hz, 2H), 7.23 (t, $J = 8.70$ Hz, 3H), 7.12 (d, $J = 7.2$ Hz, 1H), 7.01 (d, $J = 7.2$ Hz, 1H), 6.96 (t, $J = 8.1$ Hz, 1H), 5.50 (s, 1H, vinylic CH), 4.51 (s, 2H, -NCH $_2$), 3.44 (t, 2H, - $\text{CH}_2\text{CH}_2\text{CH}_3$), 1.75–1.62 (m, 2H, - $\text{CH}_2\text{CH}_2\text{CH}_3$), 0.94 (t, 3H, - CH_3); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ : 183.8 (C=O), 165.1, 162.6, 157.1, 137.7, 134.4, 128.6, 125.3, 122.8, 117.9, 115.2, 115.0, 114.7, 75.9 (vinylic CH), 52.1 (- $\text{CH}_2\text{CH}_2\text{CH}_3$), 49.0 (-NCH $_2$), 19.8 (- CH_2CH_3), 11.3 (- CH_3); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{19}\text{H}_{19}\text{FN}_2\text{O}$: 311.1559, found 311.1553.

(E)-1-(4-fluorophenyl)-2-(3-isopropyl-3,4-dihydroquinazolin-2(1H)-ylidene)ethanone (4e). The compound was obtained as a light yellow viscous material; yield: 82%; IR (ν_{max} cm^{-1}) (CHCl_3): 2925, 1584; $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ : 13.75 (s, 1H, -NH), 8.12 (dd, $J = 8.54$, 3.0 Hz, 2H), 7.44 (t, $J = 8.54$ Hz, 2H), 7.34–7.23 (m, 3H), 7.18 (d, $J = 7.32$ Hz, 1H), 5.10 (s, 1H, vinylic CH), 4.84 (s, 2H, -NCH $_2$), 4.24 (q, $J = 6.41$ Hz, 1H, -NCH), 1.25 (d, $J = 6.41$ Hz, 6H, 2 \times CH_3); $^{13}\text{C NMR}$ (100 MHz, DMSO- d_6) δ : 191.1 (C=O), 166.9, 164.4, 156.5, 135.3, 133.1, 131.7, 131.4, 128.9, 126.8, 126.5, 117.6, 116.1, 115.9, 115.7, 79.0 (vinylic CH), 52.3 (-NCH), 41.5 (-NCH $_2$), 18.6 (- CH_3); HRMS (ESI) ($\text{M} + \text{H}$) $^+$ calcd for $\text{C}_{19}\text{H}_{19}\text{F}_2\text{O}$: 311.1559, found 311.1553; ESI-MS (m/z).



(E)-2-(3-butyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4f). The compound was obtained as a light yellow solid, yield: 92%; mp 108–110 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2924, 1590; ¹H NMR (400 MHz, DMSO-d₆) δ : 13.89 (s, 1H, NH), 7.93 (dd, J = 9.0, 3.3 Hz, 2H), 7.23 (t, J = 9.0 Hz, 3H), 7.13 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 5.49 (s, 1H, vinylic CH), 4.51 (s, 2H, -NCH₂), 3.47 (t, 2H, CH₂CH₂CH₂CH₃), 1.65 (q, 2H, CH₂CH₃), 1.44–1.32 (m, 2H, -CH₂CH₂CH₃), 0.94 (t, 3H, -CH₃); ¹³C NMR (100 MHz, CDCl₃) δ : 183.7 (C=O), 165.1, 162.6, 157.0, 137.7, 134.5, 128.6, 125.3, 122.8, 117.9, 115.2, 115.0, 114.7, 75.8 (vinylic CH), 50.3 (-CH₂-CH₂CH₂CH₃), 48.9 (-NCH₂), 28.4 (-CH₂CH₂CH₃), 20.1 (-CH₂CH₃), 13.8 (-CH₃); HRMS (ESI) (M + H)⁺ calcd for C₂₀H₂₁FN₂O: 325.1716, found 325.1724.

(E)-2-(3-tert-butyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4g). The compound was obtained as a light yellow solid, yield: 86%; mp 106–108 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2925, 1581; ¹H NMR (400 MHz, DMSO-d₆) δ : 14.3 (s, 1H, NH), 7.83 (dd, J = 9.16, 3.66 Hz, 2H), 7.23–7.17 (m, 4H), 6.97 (t, J = 7.32 Hz, 1H), 6.93 (d, J = 7.93 Hz, 1H), 5.60 (s, 1H, vinylic CH), 4.34 (s, 2H, -NCH₂), 1.51 (s, 9H, 3 × CH₃); ¹³C NMR (100 MHz, DMSO-d₆) δ : 182.9 (C=O), 159.0, 137.8, 135.4, 128.6, 124.6, 122.9, 121.6, 115.1, 114.8, 82.4 (vinylic CH), 57.1 (-NCH₂), 43.9 (-C(CH₃)₃), 29.7 (-CH₃); HRMS (ESI) (M + H)⁺ calcd for C₂₀H₂₁FN₂O: 325.1716, found 325.1716.

(E)-2-(3-cyclopropyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4h). The compound was obtained as a yellow viscous material; yield: 70%; IR (ν_{\max} cm⁻¹) (CHCl₃): 2924, 1595; ¹H NMR (400 MHz, DMSO-d₆) δ : 13.5 (s, 1H, NH), 7.87 (dd, J = 8.79, 2.93 Hz, 2H), 7.18 (t, J = 7.32 Hz, 1H), 7.06 (t, J = 8.79 Hz, 2H), 7.00–6.95 (m, 2H), 6.91 (d, J = 8.05 Hz, 1H), 5.82 (s, 1H, vinylic CH), 4.37 (s, 2H, -NCH₂), 2.60–2.55 (m, 1H, -NCH), 1.00–0.96 (q, 2H, cyclopropyl CH₂), 0.81–0.79 (m, 2H, cyclopropyl CH₂); ¹³C NMR (100 MHz, CDCl₃) δ : 184.2 (C=O), 165.2, 162.7, 159.2, 137.4, 134.1, 128.7, 125.3, 122.8, 119.2, 115.1, 115.0, 114.8, 77.9 (vinylic CH), 48.7 (-NCH₂), 30.5 (-NCH), 9.0 (cyclopropyl CH₂); HRMS (ESI) (M + H)⁺ calcd for C₁₉H₁₇FN₂O: 309.1403, found 309.1405.

(E)-2-(3-cyclohexyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4i). The compound was obtained as a light yellow solid, yield: 71%; mp 116–118 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2927, 2360, 1584; ¹H NMR (400 MHz, CDCl₃) δ : 13.97 (s, 1H, NH), 7.82 (dd, J = 8.79, 2.93 Hz, 2H), 7.24–7.17 (m, 3H), 7.06 (t, J = 8.79 Hz, 1H), 7.00–6.93 (m, 2H), 5.38 (s, 1H, vinylic CH), 4.30 (s, 2H, -NCH₂), 3.80–3.74 (m, 1H, -NCH), 1.76–1.60 (m, 6H), 1.47–1.38 (m, 2H), 1.26–1.15 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ : 183.9 (C=O), 165.1, 162.6, 157.8, 137.9, 134.9, 128.6, 125.2, 122.8, 118.7, 115.0, 114.8, 75.9 (vinylic CH), 56.5 (-NCH), 41.7 (-NCH₂), 29.5 (-NCHCH₂), 25.7 (-NCHCH₂CH₂CH₂), 25.4 (-NCHCH₂CH₂CH₂); HRMS (ESI) (M + H)⁺ calcd for C₂₂H₂₃FN₂O: 351.1872, found 351.1892.

(E)-2-(1-benzyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluorophenyl)ethanone (4j). The compound was obtained as a light yellow viscous material; yield: 68%; IR (ν_{\max} cm⁻¹) (CHCl₃): 2937, 1592; ¹H NMR (400 MHz, CDCl₃) δ : 13.8 (s, 1H, NH), 7.76 (dd, J = 8.79, 2.93 Hz, 2H), 7.39–7.31 (m, 6H), 7.21 (t, J

= 7.32 Hz, 1H), 7.03–6.96 (m, 3H), 6.92 (t, J = 7.32 Hz, 1H), 5.46 (s, 1H, vinylic CH), 4.61 (s, 2H, -NCH_{2,ring}), 4.41 (s, 2H, -NHCH₂); ¹³C NMR (100 MHz, CDCl₃) δ : 184.3 (C=O), 165.2, 162.7, 157.5, 137.4, 134.9, 134.2, 130.3, 129.0, 128.6, 127.9, 126.8, 125.4, 123.0, 117.9, 115.4, 115.0, 114.7, 76.3 (vinylic CH), 48.7 (-NCH₂), 44.5 (-NCH_{2,ring}); HRMS (ESI) (M + H)⁺ calcd for C₂₃H₁₉FN₂O: 359.1559, found 359.1583.

(E)-2-(3-cyclohexyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluoro-2-methoxy phenyl)ethanone (4k). The compound was obtained as a light yellow solid, yield: 65%; mp 148–150 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2937, 1580; ¹H NMR (400 MHz, CDCl₃) δ : 13.86 (s, 1H, NH), 7.68 (t, J = 8.54 Hz, 1H), 7.18 (t, J = 6.71 Hz, 1H), 6.98–6.90 (m, 3H), 6.73–6.61 (m, 2H), 5.47 (s, 1H, vinylic CH), 4.28 (s, 2H, -NCH₂), 3.85 (s, 3H, Ar-OCH₃), 3.73–3.68 (m, 1H, -NCH), 1.72–1.54 (m, 6H), 1.40–1.30 (m, 2H), 1.26–1.13 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ : 183.7 (C=O), 165.1, 162.7, 158.2, 157.5, 134.9, 131.8, 128.5, 128.1, 125.2, 122.6, 118.6, 115.1, 107.0, 106.7, 99.4, 99.1, 81.0 (vinylic CH), 56.4 (-NCH), 55.8 (Ar-OCH₃), 41.6 (-NCH₂), 29.5 (-NCHCH₂), 25.7 (-NCHCH₂CH₂CH₂), 25.4 (-NCHCH₂CH₂CH₂); HRMS (ESI) (M + H)⁺ calcd for C₂₁H₂₃FN₂O₂: 381.1978, found 381.1975.

(E)-2-(3-butyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluoro-2-methoxyphenyl)ethanone (4l). The compound was obtained as a light brown solid, yield: 82%; mp 102–104 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2924, 1584; ¹H NMR (400 MHz, CDCl₃) δ : 13.66 (s, 1H, NH), 7.65 (t, J = 7.34 Hz, 1H), 7.22–7.14 (m, 1H), 6.94–6.88 (m, 3H), 6.65–6.60 (m, 2H), 5.36 (s, 1H, vinylic CH), 4.40 (s, 2H, -NCH₂), 3.83 (s, 3H, Ar-OCH₃), 3.28 (t, J = 7.34 Hz, 2H, -CH₂-CH₂CH₂CH₃), 1.75–1.67 (m, 2H, CH₂CH₂CH₂CH₃), 1.40–1.34 (m, 2H, CH₂CH₃), 0.98–0.91 (m, 3H, -CH₃); ¹³C NMR (100 MHz, CDCl₃) δ : 183.7 (C=O), 158.1, 156.6, 153.6, 134.5, 131.0, 128.6, 125.2, 122.6, 115.3, 107.0, 106.7, 99.4, 99.1, 80.9 (vinylic CH), 55.8 (Ar-OCH₃), 50.4 (-NCH_{2,ring}), 29.6 (-CH₂CH₂CH₂CH₃), 20.1 (-CH₂CH₃), 13.8 (-CH₃); HRMS (ESI) (M + H)⁺ calcd for C₂₁H₂₃FN₂O₂: 355.1822, found 355.1820.

(E)-2-(3-cyclopropyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-fluoro-2-methoxy phenyl)ethanone (4m). The compound was obtained as a light brown solid, mp 108–110 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2928, 1588; ¹H NMR (400 MHz, yield: 82%; CDCl₃) δ : 13.53 (s, 1H, NH), 7.67 (t, J = 8.70 Hz, 1H), 7.61 (t, J = 7.79 Hz, 1H), 6.96 (t, J = 7.33 Hz, 1H), 6.91 (d, J = 7.79 Hz, 1H), 6.88 (d, J = 7.79 Hz, 1H), 6.67 (dd, J = 8.70, 2.29 Hz, 1H), 6.65–6.61 (m, 1H), 5.84 (s, 1H, vinylic CH), 4.34 (s, 2H, -NCH₂), 3.84 (s, 3H, Ar-OCH₃), 2.52–2.45 (m, 1H, -NCH), 0.92–0.87 (q, 2H, cyclopropyl CH₂), 0.79–0.75 (m, 2H, cyclopropyl CH₂); ¹³C NMR (100 MHz, CDCl₃) δ : 184.4 (C=O), 165.2, 162.8, 158.8, 158.3, 134.3, 131.1, 128.5, 127.8, 125.3, 122.6, 119.2, 115.1, 106.9, 99.4, 83.0 (vinylic CH), 55.7 (Ar-OCH₃), 48.7 (-NHCH₂), 30.5 (-NCH), 8.8 (cyclopropyl CH₂); HRMS (ESI) (M + H)⁺ calcd for C₂₀H₁₉FN₂O₂: 339.1509, found 339.1498.

(E)-2-(3-butyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-(trifluoromethyl)phenyl)ethanone (4n). The compound was obtained as a light yellow solid, yield: 80%; mp 114–116 °C; IR (ν_{\max} cm⁻¹) (CHCl₃): 2925, 1586; ¹H NMR (400 MHz, CDCl₃) δ : 13.76 (s, 1H, NH), 7.90 (d, J = 7.79 Hz, 2H), 7.63 (d, J = 7.79 Hz, 2H), 7.24–7.18 (m, 1H), 6.98–6.92 (m, 3H), 5.34 (s, 1H, vinylic CH), 4.45 (s, 2H, -NCH₂), 3.37 (t, J = 7.33 Hz, 3H,



–CH₂CH₂CH₂CH₃), 1.72 (q, *J* = 7.33 Hz, 2H, CH₂CH₂CH₃), 1.44–1.39 (q, 2H, –CH₂CH₃), 0.98 (t, *J* = 7.33 Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ: 183.3 (C=O), 157.2, 145.1, 134.2, 128.8, 126.8, 125.4, 125.1, 123.1, 117.8, 115.4 (vinylic CH), 50.4 (–NCH₂), 49.0 (–CH₂CH₂CH₂CH₃), 28.5 (CH₂CH₂CH₃), 20.1 (–CH₂CH₃), 13.8 (CH₃); HRMS (ESI) (*M* + *H*)⁺ calcd for C₂₁H₂₁F₃N₂O: 375.1684, found 375.1680.

(*E*)-2-(3-cyclopropyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-(trifluoromethyl) phenyl)ethanone (4o). The compound was obtained as a fluorescent yellow solid; yield: 65%; mp 123–125 °C; IR (*ν*_{max} cm^{–1}) (CHCl₃): 2923, 1590; ¹H NMR (400 MHz, CDCl₃) δ: 13.6 (bs, 1H, NH), 7.95 (d, *J* = 8.24 Hz, 2H), 7.64 (d, *J* = 8.24 Hz, 2H), 7.20 (t, *J* = 7.79 Hz, 1H), 7.01–6.92 (m, 3H), 5.86 (s, 1H, vinylic CH), 4.41 (s, 2H, –NCH₂), 2.60 (m, 1H, –NCH), 1.02–0.97 (q, *J* = 5.50 Hz, 2H, cyclopropyl CH₂), 0.83–0.79 (m, 2H, cyclopropyl CH₂); ¹³C NMR (100 MHz, CDCl₃) δ: 183.7 (C=O), 159.4, 144.6, 133.9, 128.7, 126.9, 125.4, 125.1, 123.1, 119.1, 115.3, 78.7 (vinylic CH), 48.7 (–NCH₂), 30.6 (–NCH), 9.0 (cyclopropyl CH₂); HRMS (ESI) (*M* + *H*)⁺ calcd for C₂₀H₁₇F₃N₂O: 359.1371, found 359.1394.

(*E*)-2-(3-cyclohexyl-3,4-dihydroquinazolin-2(1H)-ylidene)-1-(4-(trifluoromethyl) phenyl)ethanone (4p). The compound was obtained as a light yellow viscous material; yield: 66%; IR (*ν*_{max} cm^{–1}) (CHCl₃): 2928, 1584; ¹H NMR (400 MHz, CDCl₃) δ: 13.96 (s, 1H, NH), 7.91 (d, *J* = 8.39 Hz, 2H), 7.64 (d, *J* = 8.39 Hz, 2H), 7.26–7.18 (m, 1H), 7.00–6.94 (m, 3H), 5.41 (s, 1H, vinylic CH), 4.32 (s, 2H, –NCH₂), 3.81–3.74 (m, 1H, –NCH), 1.92–1.84 (m, 3H), 1.64–1.60 (m, 1H), 1.43–1.39 (m, 2H), 1.26–1.21 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ: 183.4 (C=O), 157.9, 145.1, 134.6, 131.5, 131.1, 128.7, 126.8, 125.3, 125.1, 123.1, 118.5, 115.1, 76.9 (vinylic CH), 56.6 (–NCH), 41.8 (–NCH₂), 29.5 (–NCHCH₂), 25.7 (–NCHCH₂CH₂CH₂), 25.3 (–NCHCH₂CH₂CH₂); HRMS (ESI) (*M* + *H*)⁺ calcd for C₂₃H₂₃F₃N₂O: 401.1840, found 401.1832.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

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