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TBHP as the methyl source under Metal-free Aerobic conditions for the synthesis of Quinazolin-4(3*H*)-ones and Quinazolines via Oxidative Amination of C(sp3)-H Bond

Sushobhan Mukhopadhyay,[a,¥] Dinesh S. Barak,[a,¥] and Sanjay Batra*[a,b]

Abstract: The use of *tert*-butyl hydrogen peroxide (TBHP) as the methyl source under metal-free aerobic conditions for carrying out the oxidative amination of the C(sp3)-H bond toward synthesis of quinazolin-4(3*H*)-ones from 2-aminobenzamides and quinazolines from 2-carbonyl substituted anilines is described.

Introduction

The quinazolin-4(3*H*)-one core is a privileged heterocycle ubiquitously found in natural products[1] and compounds with diverse pharmacological activities.[2] A few representative natural compounds L-Vasicinone, Rutaecarpine, Luotonin E, (–)-Curcumadatin H and (–)-Benzomalvin C and bioactives are shown in Fig. 1. Out of several strategies for the synthesis of this scaffold,[3] the one from 2-aminobenzamides via oxidative amination of C(sp3)-H bond has received considerable attention in the recent past (Scheme 1). Such oxidative amination in 2-aminobenzamides has been realized via a variety of one carbon source including toluene,[4a] dicumyl peroxide,[4b] alcohol,[4c,d] enaminone,[4e] heterocyclic analogs,[5a-c] tertiary amine,[5d] acetophenone,[5e] alkyl acetoacetate[5f] and isonitrile[5g] both under metal-mediated and metal-free conditions.

On the other hand, *tert*-butyl hydrogen peroxide (TBHP), which is widely used as oxidant has been also reported to be a source of radical methyl group in the presence of copper catalyst. Mao et al. first disclosed an effective synthesis of methyl esters from benzylic alcohols, aldehydes or acids via copper-catalyzed C-C bond cleavage of TBHP (Fig. 2).[6] Subsequently, Li et al. developed copper-catalyzed synthesis of methyl esters from aromatic aldehydes and benzylic alcohols in the presence of TBHP.[7] Recently, Wang and co-workers reported copper-catalyzed *S*-methylation of sulfonyl hydrazides with TBHP in water for preparing methyl sulphones.[8] Use of TBHP as the methyl source is also listed during the screening of peroxide-variants in several reports.[9] For example, Zou et al.[9a] recently

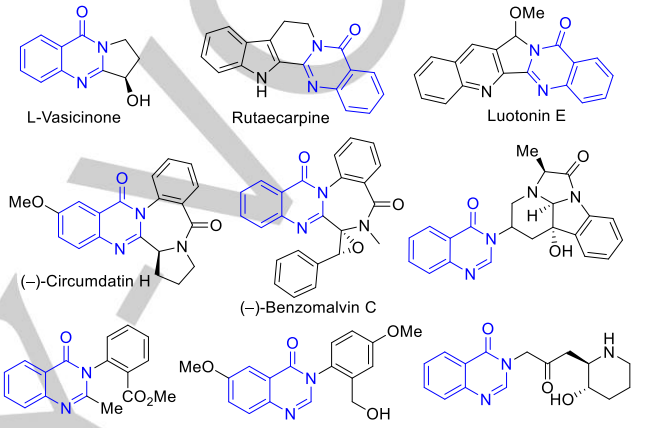

Figure 1. Natural and bioactive compounds containing quinazolin-4(3*H*)-one core.

disclosed copper (I) chloride-catalyzed methylation of 1,3-diketone by TBHP in 30% yield only in 24 h whereas Wang and co-workers disclosed the formation of quinazolin-4(3*H*)-one in 20% yield via copper (II) acetate-mediated radical methylation of 2-aminobenzamides.[4b] But TBHP was discarded in favour of peroxybenzoate and dicumyl peroxide, respectively in these studies. Song and Li et al. examined the potential of TBHP as the methyl source during their study related to metal-free oxidative 1,2-arylmethylation cascade of *N*-(arylsulfonyl)acrylamide for the assembly of 2,2-disubstituted-*N*-arylbutanamide but ditertiary butyl peroxide was found to be relatively efficient for their methodology.[9b] We noticed that though TBHP was used as efficient oxidant in a few of these protocols, there is lack of report related to efficient use of TBHP as the methyl source under metal-free conditions. Since metal-free protocols are considered to be sustainable, we sought to explore the possibility of oxidative amination of C(sp3)−H bond in 2-aminobenzamide for preparing quinazolin-4(3*H*)-ones with TBHP as the methyl source and herein we present successful results related to this study. The scope of the developed protocol was extended for preparing quinazolines from 2-carbonyl substituted anilines in the presence of NH_4OAc as the nitrogen source under metal-free conditions.

Results and Discussion

Initially, in a pilot reaction 2-amino-*N*-(4-(*tert*-

[a] S. Mukhopadhyay, D. S. Barak, S. Batra*
Medicinal and Process Chemistry Division,
CSIR-Central Drug Research Institute,
Sector 10, Jankipuram extension, Sitapur Road, Lucknow-226031
E-mail: batra_san@yahoo.co.uk, s_batra@cdri.res.in
http://www.cdri.res.in/1426.aspx?id=1426
[b] Academy of Innovative Scientific Research, New Delhi, 110025
¥Both authors have contributed equially to this work.

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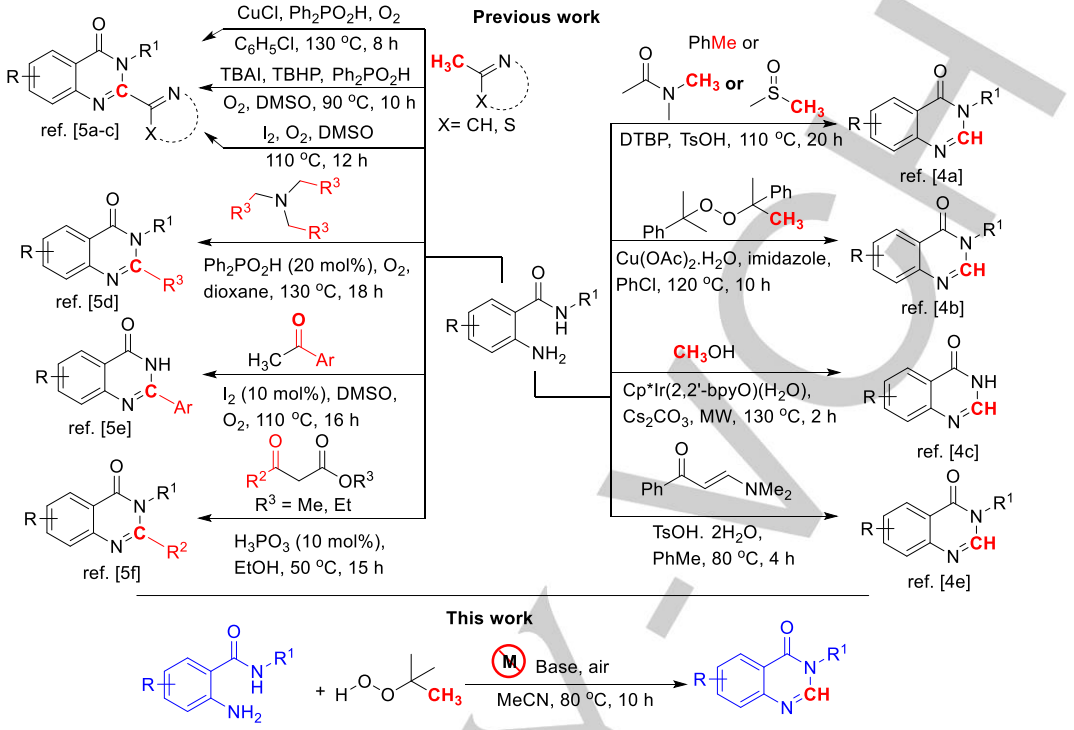


Scheme 1. Reported strategies for the synthesis of quinazolin-4(3*H*)-one via oxidative amination of C(sp3)−H bond.

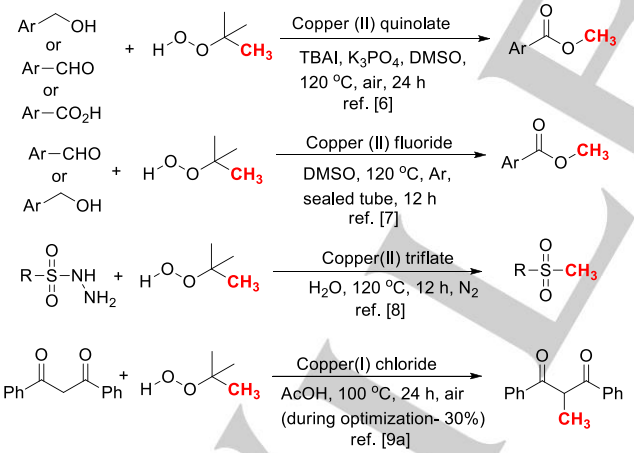
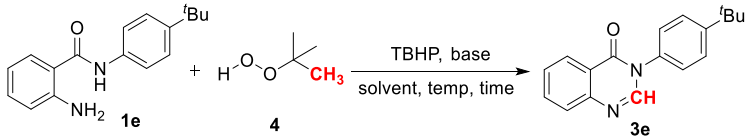


Figure 2. TBHP as methyl source in the presence of copper-catalyst.

butyl)phenyl)benzamide **1e** was treated with TBHP (5.0 equiv), Cs_2CO_3 (1.0 equiv) in DMF as the medium at room temperature but the reaction failed. Repeating the reaction at 100 °C and working it up after 24 h, however resulted in isolation of a product (36% yield) together with unreacted starting material. This product was delineated to be the quinazolin-4(3*H*)-one **(3e)** (Table 1, entry 2). This result suggested that contrary to the literature,[6-9] the presence of metal catalyst was not essential for TBHP to act as methyl source. To exclude DMF as the carbon source, we next assessed acetonitrile as the medium under identical condition which led to isolation of **3e** in 38% yield (entry 3). But as the reaction still did not go to completion, the loading of TBHP was increased to 10 equiv in the next experiment and pleasingly now the reaction was completed in 10 h to afford **3e** in 81% yield (entry 4). Screening of solvents revealed that **3e** was isolated in inferior yield when DMF, DMSO or toluene was used as the medium whereas no product was detected in THF as the medium (entries 5-8). Among different inorganic bases screened, we observed that Cs_2CO_3 was the most efficient one (compare entry 4 with entries 9-10) but lowering its loading to 0.5 equiv resulted into drop in yield (72%) of **3e** (entry 11). Further, the reaction was successful even in the absence of base to afford 48% of **3e** (entry 12). To ascertain whether air acts as co-oxidant in the reaction, we evaluated the reaction in the presence of nitrogen and oxygen atmosphere. Whereas the yield of **3e** was <5% for the reaction performed under nitrogen, the reaction conducted under oxygen was completed in 8 h to afford **3e** in 82% yield (entries 14-15). Since there was no remarkable difference between the yield of **3e** obtained from reaction performed under oxygen and the one carried out in open air, we persisted with reaction in the open flask. Thus the condition identified to obtain quinazolin-4(3*H*)-one in optimal yield was heating **1e** with 10 equiv of TBHP (70% aq), 1.0 equiv of Cs_2CO_3 in acetonitrile as the medium at 80 °C for 10 h.

Table 1. Results of the optimization study for transforming 2-aminobenzamide **(1e)** into quinazolin-4(3*H*)-one **(3e)**[a]

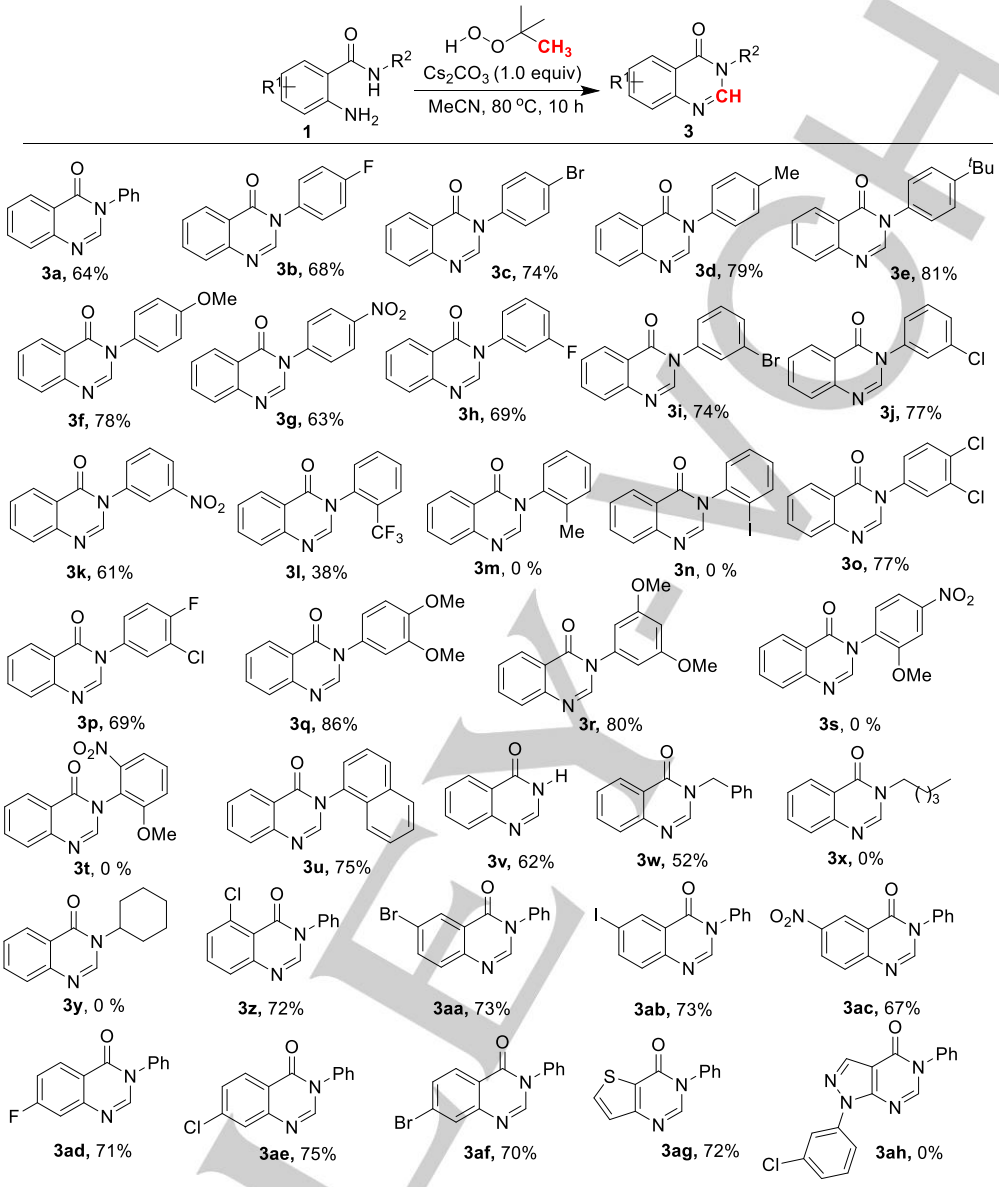


entry	TBHP (equiv)	solvent	base (equiv)	temp (°C)	time (h)	**3e** yield (%)[b]
1[c]	5.0	DMF	Cs_2CO_3 (1.0)	rt	24	ND[d]
2[c]	5.0	DMF	Cs_2CO_3 (1.0)	100	24	36
3[c]	5.0	MeCN	Cs_2CO_3 (1.0)	80	24	38
4	**10.0**	**MeCN**	**Cs_2CO_3 (1.0)**	**80**	**10**	**81**
5	10.0	DMSO	Cs_2CO_3 (1.0)	100	10	73
6	10.0	THF	Cs_2CO_3 (1.0)	70	10	ND
7	10.0	Toluene	Cs_2CO_3 (1.0)	100	10	11
8	10.0	DMF	Cs_2CO_3 (1.0)	100	10	77
9	10.0	MeCN	Na_2CO_3 (1.0)	80	10	70
10	10.0	MeCN	K_2CO_3 (1.0)	80	10	77
11	10.0	MeCN	Cs_2CO_3 (0.5)	80	10	72
12	10.0	MeCN	–	80	10	48
13	–	MeCN	Cs_2CO_3 (1.0)	80	10	ND
14[e]	10.0	MeCN	Cs_2CO_3 (1.0)	80	10	4
15[f]	**10.0**	**MeCN**	**Cs_2CO_3 (1.0)**	**80**	**8**	**82**

[a]All reactions were carried out using **1e** (0.1 g, 0.37 mmol), TBHP (70 wt. % in H_2O), solvent (4 mL) under heating for indicated time. [b]Isolated yields after purification. [c]Unreacted starting material recovered too. [d]ND = no product detected. [e]The reaction was conducted under nitrogen atmosphere. [f]The reaction was performed in the presence of oxygen

With the optimized conditions in hand, the scope of the protocol was tested with a variety of 2-aminobenzamides **1** and the results are summarized in Scheme 2. In the first set of reactions different 2-amino-*N*- substituted phenylbenzamides (**1a-u**) were treated with TBHP under the optimized conditions. The 2-amino-*N*-phenylbenzamide (**1a**) afforded **3a** in 64% yield but the formation of products for substrates bearing substituted phenyl ring was influenced by the electronic nature and position of the substituent. The substrates **(1b-1k)** with monosubstituted phenyl ring carrying the substitution at the para or meta-positions smoothly afforded the corresponding quinazolin-4-ones **(3b-k)**. The yields of products were observed to be superior for the substrates bearing electron donating substituents as compared to the electron withdrawing substituents. However, except for **1l** bearing ortho-trifluoromethyl group that gave **3l** in 38% yield, other substrates **1m-n** bearing ortho substiuents failed to furnished the product. Likewise for substrates bearing disubstituted phenyl ring, while **1o-r** afforded the respective quinazolin-4(3*H*)-one **3o-r** in 69-86% yields, **1s-t** failed to afford the corresponding products **3s-t**. Next the scope was investigated with substrates **1u-y** wherein the phenyl group of the amide was replaced with naphthyl, hydrogen, benzyl and aliphatic group. We discovered that **1u-w** gave the respective products **3u-w** but the amides bearing aliphatic groups failed to react following the protocol. Subsequently the scope was tested with substituted benzamides derivatives **1z-1af** and it was gratifying to note that all substrates afforded respective products **3z-3af** in 67-75% yields. Finally, we investigated the scope with heterocyclic substrates and found that whereas **1ag** gave the product **3ag**, **1ah** failed to afford the product **3ah**.

In order to gain insight into the plausible mechanism a few more control experiments were performed (Scheme 3). First the reaction of **1a** with TBHP was assessed in the presence of radical quenchers including TEMPO and BHT and it was found that the formation of product was impaired suggesting a radical pathway similar to the report of Wang et al.[8] The LCMS profiling



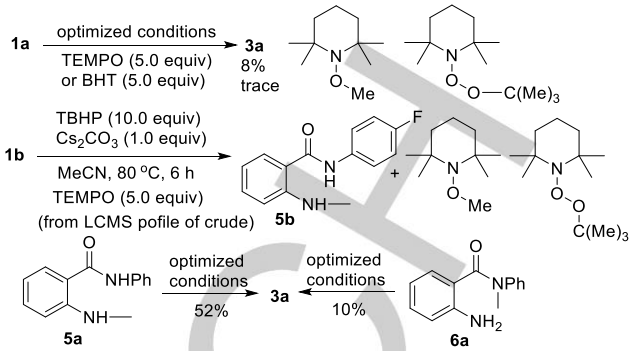
Scheme 2. Scope of the TBHP-mediated synthesis of quinazolin-4(3*H*)-one from 2-aminobenzamides. All reactions were performed at 0.2 g scale.

of the crude reaction mixture indicated the presence of molecular ion peaks corresponding to methyl-TEMPO and *tert*-butoxyl-TEMPO adducts together with that of product **3a**. Simultaneoulsy, **1b** was also subjected to similar reaction in the presence of TEMPO but now the reaction was arrested after 6 h. Herein, the LCMS profiling of the reaction mixture showed up the molecular ion peak corresponding to **5b** together with the peaks for **1b**, methyl-TEMPO and *tert*-butoxyl-TEMPO adducts. To ascertain whether the reaction is proceeding via the formation of *N*-methylated product, we prepared **5a** and subjected it to reaction under the optimized condition which resulted in the formation of **3a** in 52% yield. Conversely methylating the amide nitrogen to generate **6a** and subjecting it to reaction with TBHP under the optimized condition produced **3a** in 10% yield.

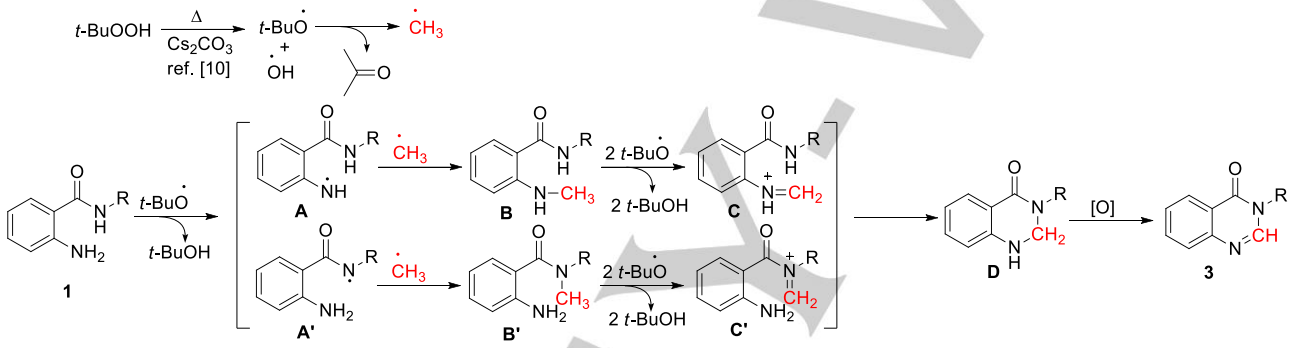
Based on these experiments a plausible mechanism via a radical pathway is outlined in Scheme 4. Initially, in the presence of Cs_2CO_3 the *tert*-butoxyl radical is formed from TBHP.[10] Under heating the *tert*-butoxyl radical affords the methyl radical with the elimination of acetone.[11] On the other hand the *tert*-butoxyl radical traps hydrogen either from the amino or the amide group of the benzamide to form intermediate **A** or **A'**. The aminyl radical reacts with the methyl radical to produce 2-(*N*-methylamino)- benzamide **B** or 2-amino-*N*-methyl-*N*-

phenylbenzamide **B'** which in the presence of *tert*-butoxyl radical loses an electron to offer iminyl cation **(C** or **C')** that undergoes intramolecular nucleophilic addition[12] to produce the tetrahydro quinazolin-4-one **D**. The intermediate **D** is oxidized in air to afford the quinazolin-4(3*H*)-one **3**.

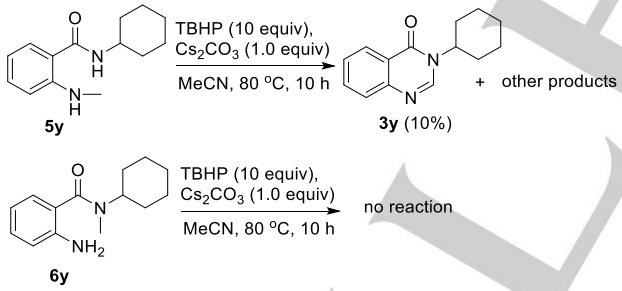
This mechanism however does not account for the failure of reaction with 2-aminobenzamide bearing *N*-aliphatic substitution. Therefore, we investigated the reaction of *N*-cyclohexyl-2-(methylamino)benzamide **(5y)** and 2-amino-N-cyclohexyl-*N*-methylbenzamide **(6y)** under the optimized conditions for the formation of the product if any (Scheme 5). We discovered that whereas **6y** failed to undergo the reaction, **5y** gave a mixture of several products from which we isolated the desired product **3y** in 10% yield only. This result provided clue that the reaction proceeds via *N*-methylation followed by C-H amination and oxidation pathway.



Scheme 3. Control experiments.



Scheme 4. Plausible mechanism for the synthesis of substituted quinazolin-4(3*H*)-one from 2-amino-*N*-substitutedphenyl benzamide.



Scheme 5. Reactions of *N*-cyclohexyl-2-(methylamino)benzamide **(5y)** and 2-amino-*N*-cyclohexyl-*N*-methylbenzamide **(6y)**..

Like quinazolin-4(3*H*)-ones, synthesis of quinazolines from 2-aminobenzophenones have been accomplished using oxidative amination of C(sp3)−H bond in the presence of a nitrogen source.[13] Given the significance of quinazolines in realms of medicinal chemistry (Fig. 3)[14] and in order to enhance the usefulness of TBHP as methyl source under metal-free condition, we considered probing the synthesis of quinazolines from 2-carbonyl substituted anilines. It is worth mentioning that initially Wang et al. reported a metal-free synthesis of quinazoline from

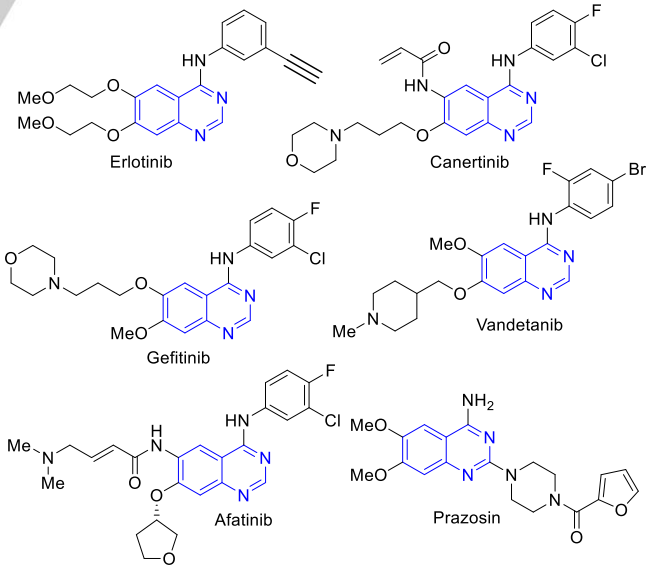
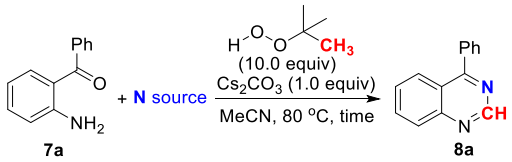


Figure 3. A few quinazoline-based anticancer drugs.

Table 2. Results of the screening of nitrogen source for the metal-free synthesis of quinazoline **8a**.[a]

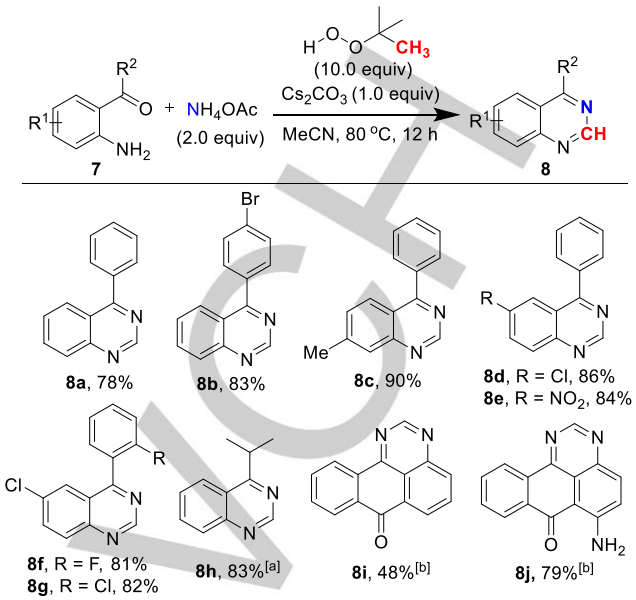


entry	Nitrogen source (equiv)	time (h)	**8a** yield (%)[b]
1	NH_3 (aq) (5.0)	12	52
2	NH_4Cl (1.0)	12	32
3	NH_4OAc (1.0)	12	61
4	**NH_4OAc (2.0)**	**12**	**78**
5	NH_4OAc (1.5)	12	70

[a] All reactions were carried out using **7a** (0.1 g, 0.51 mmol), Cs_2CO_3 (0.166 g, 0.51 mmol), TBHP (70 wt. % in H_2O), MeCN (4 mL) at 80 °C at indicated time. [b] Isolated yields after purification.

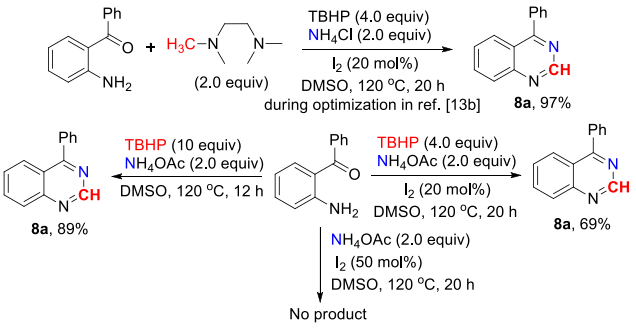
this substrate in the presence of iodine, ammonia, TBHP and dimethylacetamide (DMA).[13a] Whereas ammonia served as the nitrogen source, the carbon was derived from DMA. Subsequently, in a minor variation to this protocol, Yan et al. prepared similar quinazolines using NH_4Cl as the nitrogen source and TMEDA as the carbon source in the presence of oxygen.[13b] Strikingly however, they did not detect any product if the reaction was conducted in the presence of NIS (20 mol%), TBHP (4.0 equiv) and ammonia (2.0 equiv) as nitrogen source and DMSO as the medium. Contrary to this observation, we discovered that if the reaction of 2-aminobenzophenone **(7a)** is performed in the presence of TBHP (10.0 equiv), Cs_2CO_3 (1.0 equiv) and ammonia aqueous (25%, 5.0 equiv) in MeCN as the medium, quinazoline **8a** was isolated in 52% yield after 10 h of reaction time (Table 2, entry 1). Buoyed by this success we considered optimizing the nitrogen source in this reaction. It was found that the reaction was incomplete in the presence of NH_4Cl even after 12 h and **8a** could be isolated in 32% yield only (entry 2). However, performing the reaction by using NH_4OAc (1.0 equiv) as the nitrogen source gave **8a** in 61% yield together with recovery of the starting material. Increasing the amount of NH_4OAc to 2.0 equiv and keeping all other condition constant, the reaction was completed in 12 h to furnish **8a** in 78% yield (entry 4).

Next we tested the scope of the protocol by including a variety of 2-carbonyl substituted anilines (**7a-g)** (Scheme 6). It was gratifying to note that all substrates afforded the respective quinazolines **8a**-**8g** in 78-90% yields. Replacing phenyl group with isopropyl as in **7h**, afforded the corresponding quinazoline **8h** in 83% yield. The scope was finally evaluated with 1-aminoanthraquinone **(7i)** and 1,4-diaminoanthraquinone **(7j)** to give the corresponding perimidin-7-one derivatives **(8i-j)** in 48% and 79% yields, respectively.

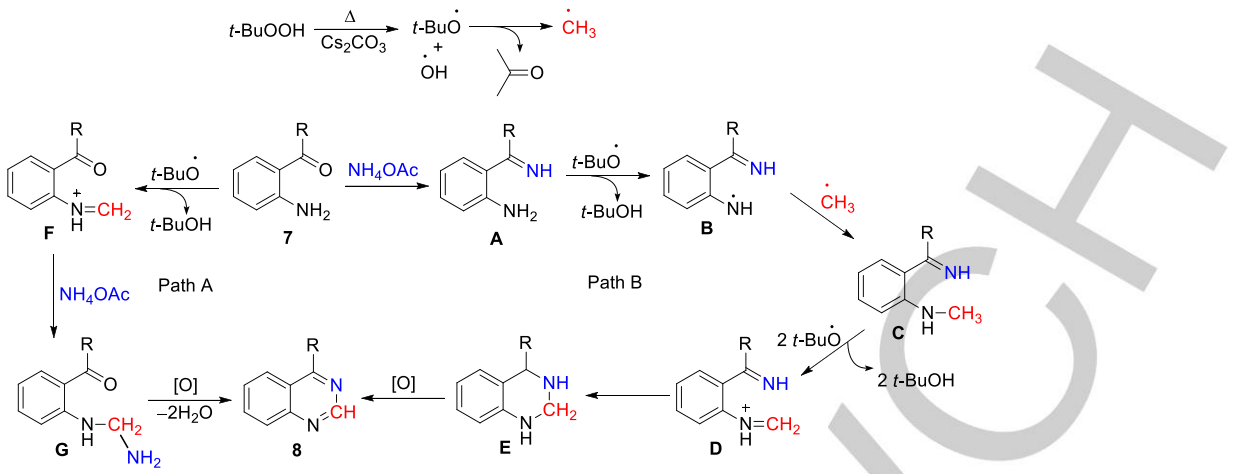


Scheme 6. Scope of the synthesis of quinazoline in the presence of TBHP under metal-free conditions. All reactions were performed at 0.2 g scale. [a] The time required for this reaction is 5 h. [b] The time required for these reactions is 24 h.

In the light of reported work,[13b] the present results generated interest to study the fate of reaction of **7a** with TBHP (4.0 equiv) in the presence of iodine (0.2 equiv) and NH_4OAc (2.0 equiv) in DMSO under heating at 120 °C without the addition of TMEDA (Scheme 7). We observed that the reaction was successful to afford the quinazoline **8a** in 69% yield. This result inferred that TMEDA was not required as the methyl source if TBHP was used in the reaction. Since TBHP and I_2 both have the propensity to act as oxidant, we next investigated the same reaction in the absence of iodine but 10.0 equiv of TBHP to successfully isolate **8a** in 89% yield. However, this reaction when performed in the absence of TBHP failed to produce **8a**. Thus it is apparent that if TBHP is used in the reaction it acts both as the methyl source and oxidant and TMEDA or I_2 is not required.



Scheme 7. Experiments to demonstrate that amine and iodine are not required for the synthesis of quinazoline in the presence of TBHP..



Scheme 8. Plausible mechanism for the TBHP-mediated synthesis of quinazolines from 2-carbonyl substituted anilines.

Based on these control experiments, it is proposed that the formation of quinazoline from 2-carbonyl substituted anilines may follow either path A or path B as outlined in Scheme 8. As reported by Wang et al.,[13a] there is a possibility of initial alkylation followed by addition of amino group which then undergo intramolecular cyclization as shown for path A. Alternatively, the likelihood of simultaneous imine formation along with the formation of iminyl cation as for quinazolin-3(4*H*)-one followed by intramolecular cyclization as shown for path B is not ruled out.

Conclusions

In conclusion, we have demonstrated the use of TBHP as source of the methyl group under metal-free aerobic conditions. We have shown that the oxidative amination of the C(sp3)-H bond in 2-aminobenzamides in the presence of TBHP and a base efficiently affords quinazolin-4(3*H*)-ones. A probe into the mechanistic detail suggests that the reaction follows a radical pathway that involves one C-C bond cleavage and two C-N bond formation. The usefulness of the protocol was enhanced by demonstrating its application for the synthesis of quinazolines from 2-carbonyl substituted anilines in the presence of NH_4OAc. Whereas the scope for the synthesis of quinazolin-4(3*H*)-ones from 2-aminobenzamide excludes substrates bearing *N*-aliphatic substitution, the synthesis of quinazolines is accomplished from aliphatic as well as aromatic 2-carbonyl substituted anilines. We have also updated the literature by demonstrating that the carbon insertion could be achieved exclusively via TBHP and TMEDA is not required as reported.

Experimental Section

General. Unless otherwise stated all reactions were performed in non-dry glassware under an air atmosphere and were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates. After elution, plate was visualized under UV illumination at 254 nm for UV active materials. Further visualization was achieved by placing the plate in Iodine chamber or via spraying with $KMnO_4$ solution. The melting points were recorded on a hot stage apparatus and are uncorrected. IR spectra were recorded using a FTIR spectrophotometer. 1H NMR and 13C NMR spectra were recorded on 400 or 500 MHz NMR spectrometers with $CDCl_3$ or DMSO-d6 as solvent, using TMS as an internal standard (chemical shifts in δ). Peak multiplicities of ^{1}H-NMR signals were designated as s (singlet), brs (broad singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), m (multiplet) and coupling constants (J) are in Hz. The LC-ESI-MS were recorded on triple quadrupole Mass spectrometer. Column chromatography was performed using silica gel (100-200 mesh). Analytical grade solvents for the column chromatography were used as received.

General procedure for the synthesis of Quinazolin-4(3*H*)-ones (3a-3ah) as exemplified for the synthesis of 3e.

In a round-bottom flask containing 2-amino-*N*-(4-(*tert*-butyl)phenyl)benzamide **1e** (0.2 g, 0.74 mmol) in MeCN (6 mL) were added Cs_2CO_3 (0.241 g, 0.74 mmol) and TBHP (70% aq) (0.95 mL, 7.4 mmol) at room temperature and the mixture was heated at 80 °C for 10 h in air. After completion of the reaction (as monitored by TLC) the solvent was removed under vacuum and the residue was diluted with H_2O (20 mL) and extracted with EtOAc (3 X 20 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to offer a residue that was purified by column chromatography over silica gel using hexanes/ EtOAc (8:2, v/v) as eluent to afford the desired product **3e** (0.168 g from 0.2 g, 81%) as a white solid. **3-(4-(*tert*-Butyl)phenyl)quinazolin-4(3*H*)-one** (**3e**).[4b] Mp 120-122 °C, (Lit. mp 120-121 °C); R_f = 0.62 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1685 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.38 (s, 9H), 7.34-7.36 (m, 2H), 7.54-7.57 (m, 3H), 7.75-7.82 (m, 2H), 8.13 (s, 1H), 8.37 (dd, J_1 = 8.0 Hz, J_2 = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 31.3, 34.8, 122.4, 126.4, 126.6, 127.2, 127.6, 134.5, 134.8, 146.3, 147.9, 152.2, 160.9. MS (ESI+): *m/z* = 279.1. ESI-HR-MS calculated for $C_{18}H_{18}N_2O$ (M^++H): 279.1497, found: 279.1499.

3-Phenylquinazolin-4(3*H*)-one (**3a**).[4a] Yield: 64% (0.134 g from 0.2 g); a white solid, mp 154-155 °C, (Lit. mp 153-155 °C); R_f = 0.65 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1683 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.35-7.37 (m, 2H), 7.40-7.44 (m, 1H), 7.46-7.50 (m, 3H),

7.69-7.76 (m, 2H), 8.06 (s, 1H), 8.30 (dd, J_1 = 8.1 Hz, J_2 = 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.4, 127.0, 127.2, 127.6, 127.7, 129.1, 129.6, 134.6, 137.5, 146.1, 147.9, 160.8. MS (ESI+): *m/z* = 223.0. ESI-HR-MS calculated for $C_{14}H_{10}N_2O$ (M^++H): 223.0871, found: 223.0874.

3-(4-Fluorophenyl)quinazolin-4(3*H*)-one (**3b**).[4b] Yield: 68% (0.142 g from 0.2 g); a white solid, mp 161-163 ºC, (Lit. mp 164-166 ºC); R_f = 0.61 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1687 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.22-7.27 (m, 2H), 7.40-7.44 (m, 2H), 7.53-7.56 (m, 1H), 7.75-7.78 (m, 2H), 8.02 (s, 1H), 8.33 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 115.9 (d, *J* = 23 Hz), 121.7, 126.1, 126.7 (d, *J* = 25 Hz), 127.3 (d, *J* = 13 Hz), 132.2 (d, *J* = 18 Hz), 133.8, 144.7, 146.7, 159.6, 161.6 (d, *J* = 225 Hz). MS (ESI+): *m/z* = 241.1. ESI-HR-MS calculated for $C_{14}H_9FN_2O$ (M^++H): 241.0777, found: 241.0773.

3-(4-Bromophenyl)quinazolin-4(3*H*)-one (**3c**).[15a] Yield: 74% (0.153 g from 0.2 g); a white solid, mp 184-186 ºC, (Lit. mp 185-187 ºC); R_f = 0.66 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1680 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.32 (d, *J* = 8.7 Hz, 2H), 7.54-7.58 (m, 1H), 7.69 (d, *J* = 7.5 Hz, 2H), 7.76-7.79 (m, 2H), 8.08 (s, 1H), 8.36 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.3, 123.5, 126.9, 127.1, 128.2, 128.9, 133.3, 134.8, 136.8, 145.7, 147.4, 160.9. MS (ESI+): *m/z* = 301.2. ESI-HR-MS calculated for $C_{14}H_9BrN_2O$ (M^++H): 300.9977, found: 300.9979.

3-(*p*-Tolyl)quinazolin-4(3*H*)-one (**3d**).[4b] Yield: 79% (0.165 g from 0.2 g); a white solid, mp 152-154 ºC, (Lit. mp 150-151 ºC); R_f = 0.59 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1684 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.36 (s, 3H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.45-7.49 (m, 1H), 7.68-7.75 (m, 2H), 8.04 (s, 1H), 8.29 (dd, J_1 = 8.2 Hz, J_2 = 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 21.2, 122.4, 126.7, 127.2, 127.6, 130.2, 134.5, 134.9, 139.2, 146.3, 147.9, 160.9. MS (ESI+): *m/z* = 237.2. ESI-HR-MS calculated for $C_{15}H_{12}N_2O$ (M^++H): 237.1028, found: 237.1023.

3-(4-Methoxyphenyl)quinazolin-4(3*H*)-one (**3f**).[4b] Yield: 78% (0.162 g from 0.2 g); a white solid, mp 208-210 ºC, (Lit. mp 210-212 ºC); R_f = 0.65 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1682 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.79 (s, 3H), 6.96 (d, *J* = 8.9 Hz, 2H), 7.25 (d, *J* = 8.9 Hz, 2H), 7.45-7.49 (m, 1H), 7.67-7.74 (m, 2H), 8.04 (s, 1H), 8.29 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 55.6, 114.9, 122.4, 127.2, 127.6, 128.2, 130.2, 134.5, 146.5, 147.9, 159.9, 161.1. MS (ESI+): *m/z* = 253.1. ESI-HR-MS calculated for $C_{15}H_{12}N_2O_2$ (M^++H): 253.0977, found: 253.0975.

3-(4-Nitrophenyl)quinazolin-4(3*H*)-one (**3g**).[15b] Yield: 63% (0.131 g from 0.2 g); a white solid, mp 197-199 ºC, (Lit. mp 199-200 ºC); R_f = 0.54 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1681 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.60 (t, *J* = 7.1 Hz, 1H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.80-7.86 (m, 2H), 8.16 (s, 1H), 8.37 (d, *J* = 7.8 Hz, 1H), 8.43 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.5, 125.0, 127.3, 127.8, 128.0, 128.3, 135.2, 142.7, 144.6, 147.3, 148.3, 160.3. MS (ESI+): *m/z* = 268.1. ESI-HR-MS calculated for $C_{14}H_9N_3O_3$ (M^++H): 268.0722, found: 268.0720.

3-(3-Fluorophenyl)quinazolin-4(3*H*)-one (**3h**).[4b] Yield: 69% (0.144 g from 0.2 g); a white solid, mp 157-159 ºC, (Lit. mp 158-160 ºC); R_f = 0.59 (hexane: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1684 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.20-7.23 (m, 3H), 7.50-7.58 (m, 2H), 7.76-7.82 (m, 2H), 8.10 (s, 1H), 8.36 (dd, J_1 = 8.1, J_2 =0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 114.9 (d, *J* = 23 Hz), 116.3 (d, *J* = 21 Hz), 122.2, 122.7 (d, *J* = 3 Hz), 127.2, 127.8 (d, *J* = 18 Hz), 130.9 (d, *J* = 9 Hz), 134.8, 138.7 (d, *J* = 10 Hz), 145.5, 147.7, 160.5, 162.8 (d, *J* = 248 Hz). MS (ESI+): *m/z* = 241.1. ESI-HR-MS calculated for $C_{14}H_9FN_2O$ (M^++H): 241.0777, found: 241.0778.

3-(3-Bromophenyl)quinazolin-4(3*H*)-one (**3i**). Yield: 74% (0.153 g from 0.2 g); a white solid, mp 175-177 ºC; R_f = 0.62 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1679 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29-7.36 (m, 2H), 7.48 (t, *J* = 6.5 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.68-7.74 (m, 2H), 8.01 (s, 1H), 8.28 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.2, 123.0, 125.8, 127.2, 127.7, 127.9, 130.3, 130.9, 132.4, 134.8, 138.6, 145.4, 147.8, 160.5. MS (ESI+): *m/z* = 301.2. ESI-HR-MS calculated for $C_{14}H_9BrN_2O$ (M^++H): 300.9977, found: 300.9980.

3-(3-Chlorophenyl)quinazolin-4(3*H*)-one (**3j**).[15c] Yield: 77% (0.160 g from 0.2 g); a white solid, mp 167-169 ºC, (Lit. mp 164-166 ºC); R_f = 0.60 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1680 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.32-7.35 (m, 1H), 7.47-7.50 (m, 3H), 7.54-7.58 (m, 1H), 7.76-7.84 (m, 2H), 8.09 (s, 1H), 8.36 (dd, J_1 = 8.0 Hz, J_2 = 0.9Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 122.2, 125.3, 127.2, 127.5, 127.7, 127.9, 129.4, 130.6, 134.8, 135.3, 138.5, 145.4, 147.7, 160.5. MS (ESI+): *m/z* = 257.0. ESI-HR-MS calculated for $C_{14}H_9ClN_2O$ (M^++H): 257.0482, found: 257.0487.

3-(3-Nitrophenyl)quinazolin-4(3*H*)-one (**3k**).[15d] Yield: 61% (0.127 g from 0.2 g); a white solid, mp 153-155 ºC, (Lit. mp 154-156 ºC); R_f = 0.64 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1681 (CO) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.63 (t, *J* = 7.3 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.86-7.93 (m, 2H), 8.07 (d, *J* = 7.7 Hz, 1H), 8.23 (d, *J* = 7.5 Hz, 1H), 8.38 (d, *J* = 8.1 Hz, 1H), 8.44 (s, 1H), 8.55 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 122.3, 123.4, 124.1, 126.9, 127.9, 128.0, 131.1, 134.9, 135.4, 138.9, 147.1, 148.1, 148.5, 160.5. MS (ESI+): *m/z* = 268.1. ESI-HR-MS calculated for $C_{14}H_9N_3O_3$ (M^++H): 268.0722, found: 268.0724.

3-(2-(Trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (**3l**).[4b] Yield: 38% (0.079 g from 0.2 g); a white solid, mp 156-158 ºC, (Lit. mp 157-159 ºC); R_f = 0.62 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1685 (CO) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.47 (d, *J* = 7.8 Hz, 1H), 7.55-7.58 (m, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.75-7.85 (m, 3H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.97 (s, 1H), 8.35 (dd, J_1 = 8.0, J_2 =1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.1, 122.8 (d, *J* = 272 Hz), 127.2, 127.7, 127.7 (d, *J* = 6 Hz), 127.8, 128.6 (d, *J* = 31 Hz), 130.3, 131.0, 133.5, 134.9, 135.3, 145.6, 147.9, 160.9. MS (ESI+): *m/z* = 291.0. ESI-HR-MS calculated for $C_{15}H_9F_3N_2O$ (M^++H): 291.0745, found: 291.0744.

3-(3,4-Dichlorophenyl)quinazolin-4(3*H*)-one (**3o**).[15e] Yield: 77% (0.159 g from 0.2 g); a white solid, mp 167-169 ºC, (Lit. mp 164-166 ºC); R_f = 0.51 (hexane: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1687 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 (dd, J_1 = 8.5 Hz, J_2 = 2.5Hz, 1H), 7.55-7.59 (m, 2H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.81-7.85 (m, 1H), 8.07 (s, 1H), 8.35 (dd, J_1 = 8.0 Hz, J_2 = 1.2Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.1, 126.4, 127.2, 128.0, 129.2, 131.3, 133.7, 134.9, 136.5, 145.0, 147.7, 160.4. MS (ESI+): *m/z* = 291.0. ESI-HR-MS calculated for $C_{14}H_8Cl_2N_2O$ (M^++H): 291.0092, found: 291.0089.

3-(3-Chloro-4-fluorophenyl)quinazolin-4(3*H*)-one (**3p**).[15f] Yield: 69% (0.143 g from 0.2 g); a white solid, mp 210-212 ºC, (Lit. mp 212-214 ºC); R_f = 0.59 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1681 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42-7.44 (m, 2H), 7.54-7.58 (m, 2H), 7.76-7.83 (m, 2H), 8.13 (s, 1H), 8.38 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.4, 127.0, 127.2, 127.6, 127.7, 129.1, 129.7, 134.6, 137.5, 146.1, 147.9, 156.6 (d, *J* = 220 Hz), 160.8. MS (ESI+): *m/z*

= 275.0. ESI-HR-MS calculated for $C_{14}H_8ClFN_2O$ (M^++H): 275.0387, found: 275.0385.

3-(3,4-Dimethoxyphenyl)quinazolin-4(3*H*)-one (**3q**).[15g] Yield: 86% (0.178 g from 0.2 g); a white solid, mp 191-193 °C; R_f = 0.53 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1683 (CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 3.78 (s, 3H), 3.83 (s, 3H), 7.09 (d, J = 10.3 Hz, 2H), 7.19 (s, 1H) 7.60 (t, J = 7.1 Hz, 1H), 7.74 (d, J = 6.9 Hz, 1H), 7.88 (t, J = 6.9 Hz, 1H), 8.20 (d, J = 7.3 Hz, 1H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 56.2, 112.0, 112.1, 120.0, 122.4, 126.9, 127.7, 127.8, 130.9, 135.0, 148.0, 148.2, 149.3, 149.5, 160.6. MS (ESI+): *m/z* = 283.1. ESI-HR-MS calculated for $C_{16}H_{14}N_2O_3$ (M^++H): 283.1083, found: 283.1084.

3-(3,5-Dimethoxyphenyl)quinazolin-4(3*H*)-one (**3r**).[15h] Yield: 80% (0.166 g from 0.2 g); a white solid, mp 227-228 °C, (Lit. mp 225-228 °C); R_f = 0.60 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1681 (CO) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.75 (s, 6H), 6.48-6.50 (m, 3H), 7.48 (t, J = 7.8 Hz, 1H), 7.68-7.75 (m, 2H), 8.04 (s, 1H), 8.29 (d, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 55.6, 101.3, 105.5, 122.4, 127.2, 127.5, 127.6, 134.6, 139.1, 146.0, 147.8, 160.6, 161.4. MS (ESI+): *m/z* = 283.1. ESI-HR-MS calculated for $C_{16}H_{14}N_2O_3$ (M^++H): 283.1083, found: 283.1081.

3-(Naphthalen-1-yl)quinazolin-4(3*H*)-one (**3u**).[4b] Yield: 75% (0.156 g from 0.2 g); a white solid, mp 140-142 °C, (Lit. mp 142-144 °C); R_f = 0.59 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1686 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45-7.56 (m, 6H), 7.77-7.79 (m, 2H), 7.90 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 8.2 Hz, 1H), 8.03 (s, 1H), 8.33 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.0, 122.4, 125.5, 126.0, 126.9, 127.3, 127.7, 127.7, 127.8, 128.6, 129.8, 130.3, 134.1, 134.4, 134.7, 146.9, 148.2, 161.1. MS (ESI+): *m/z* = 273.1. ESI-HR-MS calculated for $C_{18}H_{12}N_2O$ (M^++H): 273.1028, found: 273.1025.

Quinazolin-4(3*H*)-one (**3v**).[15i] Yield: 62% (0.133 g from 0.2 g); a white solid, mp 200-201 °C, (Lit. mp 200-202 °C); R_f = 0.36 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1698 (CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.52 (t, J = 7.4 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.82 (t, J = 7.4 Hz, 1H), 8.09 (s, 1H), 8.13 (d, J = 7.8 Hz, 1H), 12.23 (brs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 123.1, 126.3, 127.2, 127.7, 134.7, 145.8, 149.2, 161.2. MS (ESI+): *m/z* = 147.0. ESI-HR-MS calculated for $C_8H_6N_2O$ (M^++H): 147.0558, found: 147.0559.

3-Benzylquinazolin-4(3*H*)-one (**3w**).[4b] Yield: 52% (0.108 g from 0.2 g); a white solid, mp 116-118 °C, (Lit. mp 117-118 °C); R_f = 0.55 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1678 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.20 (s, 2H), 7.31-7.36 (m, 5H), 7.50 (t, J = 7.5 Hz, 1H), 7.69-7.75 (m, 2H), 8.11 (s, 1H), 8.33 (d, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 49.6, 122.2, 126.9, 127.4, 127.5, 128.0, 128.3, 129.0, 134.3, 135.8, 146.3, 148.1, 161.1. MS (ESI+): *m/z* = 237.2. ESI-HR-MS calculated for $C_{15}H_{12}N_2O$ (M^++H): 237.1028, found: 237.1030.

3-Cyclohexylquinazolin-4(3*H*)-one (**3y**).[4b] Yield: 10% (0.019 g from 0.2 g); a white solid, mp 116-118 °C, (Lit. mp 118-119 °C); R_f = 0.59 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1670 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.24-1.28 (m, 1H), 1.48-1.70 (m, 4H), 1.78-1.81 (m, 1H), 1.93-2.03 (m, 4H), 4.78-4.86 (m, 1H), 7.47-7.52 (m, 1H), 7.69-7.77 (m, 2H), 8.13 (s, 1H), 8.32 (dd, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 25.3, 25.9, 32.6, 53.4, 121.9, 126.9, 127.1, 127.2, 134.1, 143.9, 147.5, 160.7. MS (ESI+): *m/z* = 229.1. ESI-HR-MS calculated for $C_{14}H_{16}N_2O$ (M^++H): 229.1341, found: 229.1338.

5-Chloro-3-phenylquinazolin-4(3*H*)-one (**3z**). Yield: 72% (0.150 g from 0.2 g); a white solid, mp 167-169 °C; R_f = 0.61 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1680 (CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.33-7.42 (m, 2H), 7.60-7.64 (m, 2H), 7.74-7.78 (m, 3H), 7.86-7.89 (m, 1H), 8.00 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 124.9, 127.0, 127.7, 128.4, 129.2, 129.3, 132.7, 134.5, 136.9, 145.9, 147.2, 160.4. MS (ESI+): *m/z* = 257.1. ESI-HR-MS calculated for $C_{14}H_9ClN_2O$ (M^++H): 257.0482, found: 257.0480.

6-Bromo-3-phenylquinazolin-4(3*H*)-one (**3aa**).[4b] Yield: 73% (0.151 g from 0.2 g); a white solid, mp 182-184 °C, (Lit. mp 185-186 °C); R_f = 0.60 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1689 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40-7.43 (m, 2H), 7.51-7.58 (m, 3H),7.64 (d, J = 8.7 Hz, 1H), 7.88 (dd, J_1 = 8.7 Hz, J_2 = 2.3 Hz, 1H), 8.13 (s, 1H), 8.49 (d, J = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 121.3, 123.8, 126.9, 129.3, 129.4, 129.8, 137.2, 137.8, 146.4, 146.7, 159.6. MS (ESI+): *m/z* = 301.2. ESI-HR-MS calculated for $C_{14}H_9BrN_2O$ (M^++H): 300.9977, found: 300.9979.

6-Iodo-3-phenylquinazolin-4(3*H*)-one (**3ab**).[15j] Yield: 73% (0.150 g from 0.2 g); a white solid, mp 132-134 °C; R_f = 0.62 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1682 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.19 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.55 (d, J = 7.8 Hz, 2H), 7.66 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 101.3, 120.5, 125.4, 125.9, 129.2, 134.0, 137.0, 137.6, 139.9, 145.7, 162.7. MS (ESI+): *m/z* = 349.0. ESI-HR-MS calculated for $C_{14}H_9IN_2O$ (M^++H): 348.9838, found: 348.9833.

6-Nitro-3-phenylquinazolin-4(3*H*)-one (**3ac**).[4b] Yield: 67% (0.139 g from 0.2 g); a white solid, mp 222-224 °C, (Lit. mp 223-225 °C); R_f = 0.56 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1679 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (d, J = 7.0 Hz, 2H), 7.54-7.61 (m, 3H), 7.90 (d, J = 8.9 Hz, 1H), 8.26 (s, 1H), 8.59 (dd, J_1= 6.4 Hz, J_2 = 2.6 Hz , 1H), 9.21 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.7, 123.8, 126.8, 128.6, 129.3, 129.7, 129.9, 136.7, 146.4, 148.9, 151.9, 159.6. MS (ESI+): *m/z* = 268.1. ESI-HR-MS calculated for $C_{14}H_9N_3O_3$ (M^++H): 268.0722, found: 268.0721.

7-Fluoro-3-phenylquinazolin-4(3*H*)-one (**3ad**).[4a] Yield: 71% (0.148 g from 0.2 g); a white solid, mp 196-198 °C, (Lit. mp 197-199 °C); R_f = 0.61 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1688 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24-7.29 (m, 1H), 7.40-7.43 (m, 3H), 7.49-7.58 (m, 3H), 8.14 (s, 1H), 8.38 (dd, J_1 = 8.9 Hz, J_2 = 0.1Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 113.1 (d, J = 22 Hz), 116.4 (d, J = 24 Hz), 119.1, 127.0, 129.3, 129.7, 130.0 (d, J = 10 Hz), 137.2, 147.4, 150.1 (d, J = 13 Hz), 160.0, 166.6 (d, J = 253 Hz). MS (ESI+): *m/z* = 241.1. ESI-HR-MS calculated for $C_{14}H_9FN_2O$ (M^++H): 241.0777, found: 241.0780.

7-Chloro-3-phenylquinazolin-4(3*H*)-one (**3ae**).[15k] Yield: 75% (0.156 g from 0.2 g); a white solid, mp 196-198 °C, (Lit. mp 197-199 °C); R_f = 0.58 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1681 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41-7.44 (m, 2H), 7.51-7.58 (m, 4H), 7.78 (s, 1H), 8.13 (s, 1H), 8.38 (d, J = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 120.9, 126.9, 127.2, 128.3, 128.7, 129.3, 129.7, 137.2, 140.9, 147.3, 148.9, 160.2. MS (ESI+): *m/z* = 257.0. ESI-HR-MS calculated for $C_{14}H_9ClN_2O$ (M^++H): 257.0482, found: 257.0485.

7-Bromo-3-phenylquinazolin-4(3*H*)-one (**3af**). Yield: 70% (0.145 g from 0.2 g); a white solid, mp 143-145 °C; R_f = 0.66 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1684 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 (d, J = 7.2 Hz, 2H), 7.50-7.56 (m, 3H), 7.65 (d, J = 8.2 Hz, 1H), 7.95 (s, 1H), 8.12 (s, 1H), 8.21 (d, J = 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 121.3, 126.9, 128.7, 129.3, 129.7, 130.4, 131.1, 137.2,

147.2, 148.9, 160.3. MS (ESI+): *m/z* = 301.1. ESI-HR-MS calculated for $C_{14}H_9BrN_2O$ (M^++H): 300.9977, found: 300.9978.

3-Phenylthieno[2,3-*d*]pyrimidin-4(3*H*)-one (**3ag**). Yield: 72% (0.150 g from 0.2 g); a white solid, mp 121-123 °C; R_f = 0.62 (hexanes: EtOAc, 7:3, v/v); IR (KBr) ν_{max}: 1678 (CO) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39 (d, *J* = 5.3 Hz, 1H), 7.42-7.44 (m, 2H), 7.49-7.58 (m, 3H), 7.85 (d, *J* = 5.3 Hz, 1H), 8.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 124.0, 125.3, 127.1, 129.3, 129.6, 134.8, 137.0, 147.5, 156.8, 156.9. MS (ESI+): *m/z* = 229.0. ESI-HR-MS calculated for $C_{12}H_8N_2OS$ (M^++H): 229.0436, found: 229.0439.

General procedure for the synthesis of Quinazolines (8a-8h) as exemplified for the synthesis of 8a.

In a round-bottom flask containing (2-aminophenyl)(phenyl)methanone **7a** (0.2 g, 1.0 mmol) in MeCN (8 mL) were added Cs_2CO_3 (0.325 g, 1.0 mmol), NH_4OAc (0.154 g, 2.0 mmol) and TBHP (70% aq) (1.3 mL, 10.0 mmol) at room temperature and the mixture was heated at 80 °C for 12 h in air. Upon completion as monitored by TLC, the solvent was removed from the reaction under vacuum and the residue was diluted with H_2O (20 mL) and extracted with EtOAc (3 X 20 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to offer a residue that was purified by column chromatography over silica gel using hexanes/ EtOAc (8:2, v/v) as eluent to afford the desired product **8a** (0.163 g from 0.2 g, 78%) as a yellow solid. **4-Phenylquinazoline** (**8a**).[13a] Mp 96-98 °C, (Lit. mp 96-97 °C); R_f = 0.56 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58-7.61 (m, 4H), 7.78-7.80 (m, 2H), 7.91-7.95 (m, 1H), 8.13-8.16 (m, 2H), 9.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 123.2, 127.2, 127.8, 128.7, 128.8, 129.9, 130.1, 133.8, 137.0, 150.9, 154.5, 168.6. MS (ESI+): *m/z* = 207.2. ESI-HR-MS calculated for $C_{14}H_{10}N_2$ (M^++H): 207.0922, found: 207.0914.

4-(4-Bromophenyl)quinazoline (**8b**).[13a] Yield: 83% (0.171 g from 0.2 g); a yellow solid, mp 150-152 °C, (Lit. mp 152-154 °C); R_f = 0.52 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61-7.65 (m, 1H), 7.66-7.69 (m, 2H), 7.71-7.74 (m, 2H), 7.91-7.96 (m, 1H), 8.08 (dd, J_1 = 8.5 Hz, J_2 = 0.6 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 9.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 122.9, 124.8, 126.6, 127.9, 129.1, 131.5, 131.9, 133.9, 136.0, 151.2, 154.6, 167.2. MS (ESI+): *m/z* = 285.1. ESI-HR-MS calculated for $C_{14}H_9BrN_2$ (M^++H): 285.0027, found: 285.0022.

7-Methyl-4-phenylquinazoline (**8c**). [15l] Yield: 90% (0.188 g from 0.2 g); a white solid, mp 94-96 °C; R_f = 0.55 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.61 (s, 3H), 7.43 (dd, J_1 = 8.6 Hz, J_2 = 1.4 Hz, 1H), 7.56-7.58 (m, 3H), 7.76-7.78 (m, 2H), 7.89 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 9.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 22.1, 121.3, 126.8, 127.8, 128.6, 129.9, 129.9, 130.0, 137.3, 144.8, 151.4, 154.8, 167.8. MS (ESI+): *m/z* = 221.2. ESI-HR-MS calculated for $C_{15}H_{12}N_2$ (M^++H): 221.1079, found: 221.1085.

6-Chloro-4-phenylquinazoline (**8d**).[13a] Yield: 86% (0.179 g from 0.2 g); a yellow solid, mp 136-137 °C, (Lit. mp 135-136 °C); R_f = 0.61 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59-7.61 (m, 3H), 7.76-7.78 (m, 2H), 7.85 (dd, J_1 = 8.9 Hz, J_2 = 2.2 Hz, 1H), 8.07 (d, *J* = 8.9 Hz, 1H), 8.11 (d, *J* = 2.2 Hz, 1H), 9.38 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 123.7, 125.8, 128.9, 129.8, 130.4, 130.7, 133.5, 134.7, 136.6, 149.6, 154.8, 167.7. MS (ESI+): *m/z* = 241.1. ESI-HR-MS calculated for $C_{14}H_9ClN_2$ (M^++H): 241.0533, found: 241.0534.

6-Nitro-4-phenylquinazoline (**8e**).[13a] Yield: 84% (0.174 g from 0.2 g); a yellow solid, mp 129-131 °C, (Lit. mp 131-132 °C); R_f = 0.58 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.59-7.67 (m, 3H), 7.82 (d, *J* = 5.1 Hz, 2H), 8.28 (d, *J* = 9.1 Hz, 1H), 8.68(d, *J* = 8.7 Hz, 1H), 9.08 (s, 1H), 9.52 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 122.1, 124.2, 127.0, 129.1, 130.1, 131.1, 131.2, 135.8, 146.2, 153.5, 157.2, 170.7. MS (ESI+): *m/z* = 252.2. ESI-HR-MS calculated for $C_{14}H_9N_3O_2$ (M^++H): 252.0773, found: 252.0771.

6-Chloro-4-(2-fluorophenyl)quinazoline (**8f**).[15l] Yield: 81% (0.168 g from 0.2 g); a white solid, mp 117-119 °C; R_f = 0.60 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.30 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 5.9 Hz, 1H), 7.59-7.61 (m, 2H), 7.80 (s, 1H), 7.86 (d, *J* = 7.1 Hz, 1H), 8.08 (d, *J* = 7.1 Hz, 1H), 9.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 116.3 (d, *J*= 21 Hz), 124.5, 124.8, 124.9, 125.6 (d, *J*= 4 Hz), 130.6, 131.5 (d, *J*= 3 Hz), 132.2 (d, *J*= 8 Hz), 133.8, 135.1, 149.1, 154.9, 159.7 (d, *J*= 249 Hz), 163.7. MS (ESI+): *m/z* = 259.1. ESI-HR-MS calculated for $C_{14}H_8ClFN_2$ (M^++H): 259.0438, found: 259.0432.

6-Chloro-4-(2-chlorophenyl)quinazoline (**8g**).[15m] Yield: 82% (0.169 g from 0.2 g); a yellow solid, mp 76-78 °C, (Lit. mp 78-80 °C); R_f = 0.65 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46-7.47 (m, 1H), 7.48-7.51 (m, 1H), 7.53-7.55 (m, 1H), 7.59-7.61 (m, 1H), 7.63 (d, *J* = 2.0 Hz, 1H), 7.86 (dd, J_1 = 9.0 Hz, J_2 = 2.3 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 9.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 124.4, 125.6, 127.2, 130.2, 130.6, 130.8, 131.1, 132.7, 133.8, 135.1, 135.4, 149.1, 154.8, 166.4. MS (ESI+): *m/z* = 275.1. ESI-HR-MS calculated for $C_{14}H_8Cl_2N_2$ (M^++H): 275.0143, found: 275.0141.

4-Isopropylquinazoline (**8h**).[13a] Yield: 83% (0.175 g from 0.2 g); a yellow oil; R_f = 0.61 (hexanes: EtOAc, 6:4, v/v); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.45 (d, *J* = 6.8 Hz, 6H), 3.91-3.98 (m, 1H), 7.62-7.66 (m, 1H), 7.86-7.89 (m, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 9.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 21.7, 30.9, 123.2, 124.1, 127.4, 129.3, 133.3, 150.0, 154.7, 175.8. MS (ESI+): *m/z* = 173.2. ESI-HR-MS calculated for $C_{11}H_{12}N_2$ (M^++H): 173.1079, found: 173.1072.

7*H*-Benzo[*e*]perimidin-7-one (**8i**).[15l,n] Yield: 48% (0.099 g from 0.2 g); a brown solid, mp 178-180 °C; R_f = 0.45 (hexanes: EtOAc, 3:7, v/v); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.88-7.92 (m, 1H), 7.98-8.02 (m, 1H), 8.25-8.29 (m, 1H), 8.35 (dd, J_1 = 6.7 Hz, J_2 = 1.0 Hz, 1H), 8.44 (dd, J_1 = 7.5 Hz, J_2 = 0.96 Hz, 1H), 8.56 (dd, J_1 = 6.3 Hz, J_2 = 0.96 Hz, 1H), 8.86 (dd, J_1 = 6.9 Hz, J_2 = 0.92 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 123.3, 124.6, 125.6, 129.8, 130.7, 132.9, 133.4, 134.7, 135.0, 135.2, 135.8, 147.2, 149.2, 152.9, 181.4. MS (ESI+): *m/z* = 233.2. ESI-HR-MS calculated for $C_{15}H_8N_2O$ (M^++H): 233.0715, found: 233.0721.

6-Amino-7*H*-benzo[*e*]perimidin-7-one (**8j**).[15o] Yield: 79% (0.164 g from 0.2 g); a brown solid, mp 272-274 °C, (Lit. mp 277-278 °C); R_f = 0.38 (hexanes: EtOAc, 2:8, v/v); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.65 (d, *J* = 9.4 Hz, 1H), 7.83-7.92 (m, 2H), 8.02 (d, *J* = 9.4 Hz, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.77 (brs, 1H), 8.89 (d, *J* = 7.6 Hz, 1H), 9.27 (s, 1H), 10.13 (brs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 102.2, 120.3, 124.9, 126.6, 129.4, 131.8, 132.9, 133.9, 134.3, 136.9, 145.5, 149.5, 152.3, 154.9, 180.9. MS (ESI+): *m/z* = 248.2. ESI-HR-MS calculated for $C_{15}H_9N_3O$ (M^++H): 248.0824, found: 248.0818.

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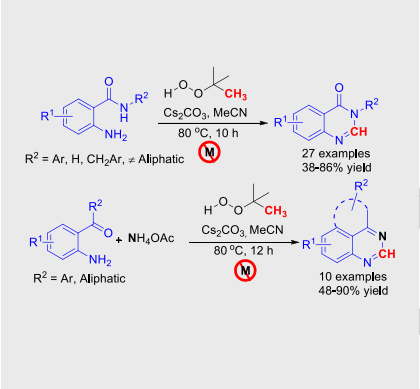
tert-Butyl hydrogen peroxide (TBHP) serves as the methyl source under metal-free aerobic conditions for carrying out the oxidative amination of the C(sp3)-H bond toward preparing quinazolin-4(3*H*)-ones and quinazolines is reported.



Nitrogen heterocycles*

*S. Mukhopadhyay, D. S. Barak, and S. Batra***

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TBHP as the methyl source under Metal-free Aerobic conditions for the synthesis of Quinazolin-4(3*H*)-ones and Quinazolines via Oxidative Amination of C(sp3)-H Bond