Iodine-promoted facile synthesis of new (±)-*N*,2-diaryl-2,3-dihydroquinazolines

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Abstract

The reactivity of 2-amino-*N'*-arylbenzamidines **1a-e** towards *p*-tolualdehyde **2a** and 1-naphthaldehyde **2b** under the catalytic influence of commercial iodine at ambient temperature has been examined. New chiral quinazolines **3a-e** and **4a-d** have been identified as reaction products. These products have subsequently been oxidised to *N*,2-diarylquinazolin-4-amines **12**, **13a-d**. The structures of the products were elucidated by their NMR, mass and IR spectra in addition to elemental analyses. The structure of **3e** was further confirmed by X-ray structural analysis. The mechanism of formation of **3a-e** and **4a-d** is discussed.

Keywords: 2-Amino-*N'*-arylbenzamidines, aldehydes, quinazolines, iodine

Introduction

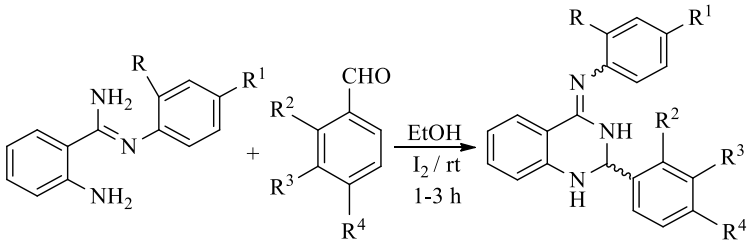
The pyrimidine nucleus is incorporated in a large number of alkaloids, drugs, antibiotics, agrochemicals, and antimicrobial agents.[1,2] Thus, many fused pyrimidine derivatives are of importance in chemistry, biology, and medicine. Their synthesis is well recognized in the literature and there exist several review articles and monographs.[3] Often the limiting factor for the above approaches is the difficulty encountered in obtaining key intermediates or their precursors in high enough yields.

This is also true for quinazolines which occupy a prominent position among these heterocycles. We have found that novel 2,4-disubstituted quinazolines could be produced in good yields under mild conditions from the reaction of 2-amino-*N'*-arylbenzamidines with tetracyanoethylene,[4] 4-formyl[2.2]paracyclophane,[5] isatoic anhydride,[6] and 2,3-dichloro-1,4-naphthoquinone.[7]

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Results and Discussion

The reaction of 2-amino-*N'*-arylbenzamidines **1a-e** with p-tolualdehyde **2a** and 1-naphthaldehyde **2b** in the presence of molecular iodine at room temperature, leads to the formation of the N,2-diarylquinazolines **3a-e** and **4a-d** in moderate to good yields (59-71%) as shown in Scheme 1. Iodine is known as an inexpensive and non-toxic weak Lewis acid, is a readily available reagent for various organic transformations and often yields products with outstanding selectivity.[8]



1a-e **2a,b** **3a-e, 4a-d**

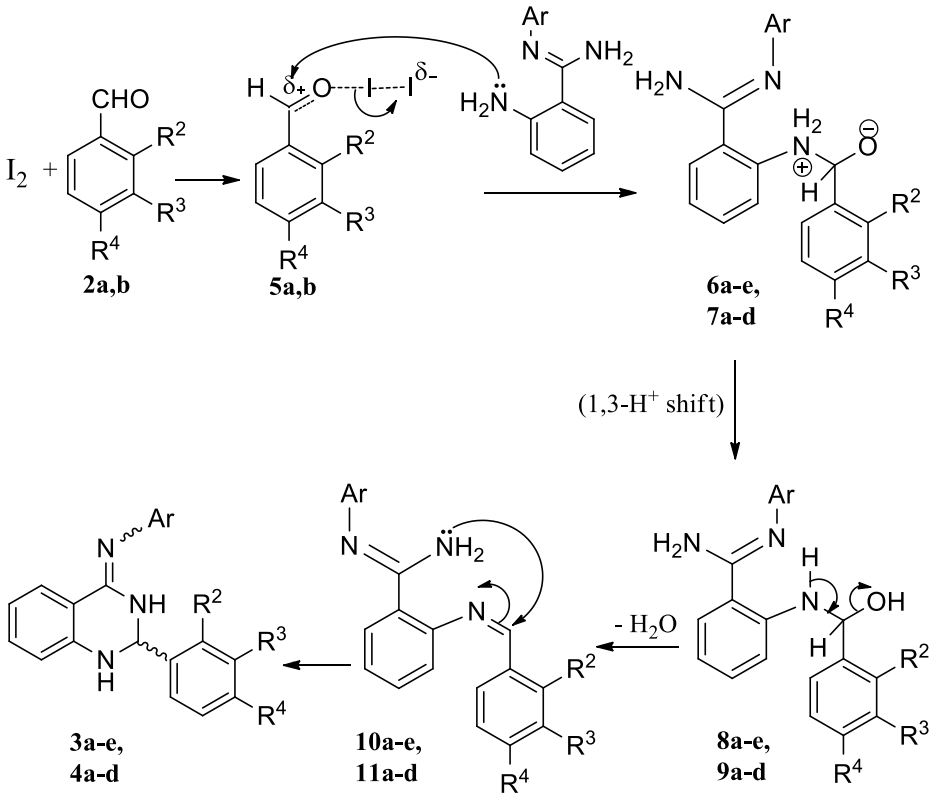
compound	**a**	**b**	**c**	**d**	**e**
1	R = R^1 = H	R = H, R^1 = CH3	R = H, R^1 = Cl	R = H, R^1 = Br	R = R^1 = CH_3
2	R^2 = R^3 = H, R^4 = CH_3	R^4 = H, R^2 = R^3 = -CH=CH-	-	-	-
3	R=R^1=R^2=R^3= H, R^4 = CH_3	R = R^2 = R^3 = H, R^1 = R^4 = CH_3	R = R^2 = R^3 = H, R^1 = Cl, R^4 = CH_3	R = R^2 = R^3 = H, R^1 = Br, R^4=CH_3	R=R^1=R^4= CH_3, R^2=R^3=H
4	R = R^1 = R^4 = H, R^2 = R^3 = -CH=CH-	R=R^4=H, R^1=CH_3, R^2=R^3= -CH=CH-	R=R^4=H, R^1=Cl, R^2=R^3=-CH=CH-	R=R^4=H, R^1=Br, R^2=R^3=-CH=CH-	-

Scheme 1. Reaction of 2-amino-*N'*-arylbenzamidines **1a-e** with *p*-tolualdehyde **2a** and 1-naphthaldehyde **2b**.

It is noted that the products **3a-e** and **4a-d** possess a centre of chirality, so this route in principle could also provide optically active compounds. We found that the presence of iodine is crucial in obtaining high yields of the corresponding products, and thus set out first to investigate the effect of the concentration of the added iodine, hoping to identify optimal conditions for the cyclization to proceed. This study revealed that a tenth equivalent of molecular iodine is sufficient to convert one equivalent of substrate **1a-e** into quinazoline derivatives **3a-e** and **4a-d**. Another important factor is the reaction temperature, and room temperature is sufficient to carry

out the conversion. In comparison with reported methods using other condensing agents,[9-11] our procedure can be carried out safely under milder conditions.

The products **3a-e** and **4a-d** as shown in Scheme 1 are produced as racemic mixtures of diasteromers. This is clearly seen in the TLC analysis (two poorly separated spots) and NMR spectra (line doubling in the ^{13}C NMR spectra). Based on the signals of the ^{1}H NMR spectrum we deduce that the diastereomers are formed in 4:1-ratio. The formation of the products **3a-e** and **4a-d** may be rationalized according to the pathway shown in Scheme 2.



Scheme 2. Mechanism suggested for the formation of the products **3a-e** and **4a-d**.

In the initial reaction the Lewis acid I2 polarizes the carbonyl group as shown by structure **5a, b**. With its reactivity enhanced the carbonyl group is attacked by the amino substituent of **1a-e** and after (1,3-H^+ shift) water is lost from **8a-e** and **9a-d** to yield the Schiff base **10a-e** and **11a-d** which finally cyclizes to **3a-e** and **4a-d**.

The structures of the main diastereoisomeric products **3a-e** were deduced from their elemental analyses and their IR, ^{1}H NMR, ^{13}C NMR and mass spectra as described in the experimental section.

As a typical example, the IR spectrum of the main diastereoisomeric product **3b** displayed two strong absorption maxima at ν = 3415 and 3257 cm^{-1}, indicating the presence of two different (NH-) groups, while the C=N group absorbs at ν = 1603 cm^{-1}. Taking the ^{1}H NMR

spectrum of the main product **3b** as an example it exhibits two broad singlets at δ = 7.03 and 4.32 ppm indicating the presence of two -NH- groups. The hydrogen atom at the chiral carbon atom (C-2) is recorded at 5.56 ppm as a sharp singlet. However, the two methyl groups of the two aryl substituents resonated as two sharp singlets at δ = 2.35 and 2.26 ppm for the *Z*-isomer and we detected another two singlets at δ = 2.40 and 2.31 ppm for the corresponding groups of the *E*-isomer. The aromatic protons (H-9, -10 and H-13, -14) produce four doublets at δ = 7.40, 7.26, 7.19 and 7.07 ppm with coupling constants *J* = 7.99 and 7.82 Hz. In addition, two multiplets at δ = 7.31-7.28 and at 6.94-6.87 ppm assignable to ArH-5, -6, -7, and -8 are registered. The ^{13}C NMR spectrum of the main product 3b showed twenty-one distinct resonance signals in agreement with the proposed structure. Two of these carbon atoms represent the methyl group carbon atoms and resonate at δ = 21.2 and 20.7 ppm. The quinazoline C-2 carbon atom of *Z*- and *E*-isomers resonated at δ = 68.4 and 68.0 ppm. Finally, the mass spectra show the molecular ion peaks in accordance with the proposed structures of **3a-e**.

The structure of compound **3e** was confirmed by X-ray structure analysis of the diethyl ether hemisolvate (Figure 1). The two independent molecules of **3e** are closely similar, differing only in the orientation of the ring system C19-26 (by ca. 10°); a least-squares fit of all other non-H atoms gave a r.m.s. deviation of 0.085 Å. The molecular packing (Figure 2) consists of chains parallel to the x axis in which the two independent molecules alternate, connected by hydrogen bonds N1-H01λN18' and N1'-H01'λN18; the ether molecule is connected to the second independent molecule by the hydrogen bond N3'-H03'λO93.

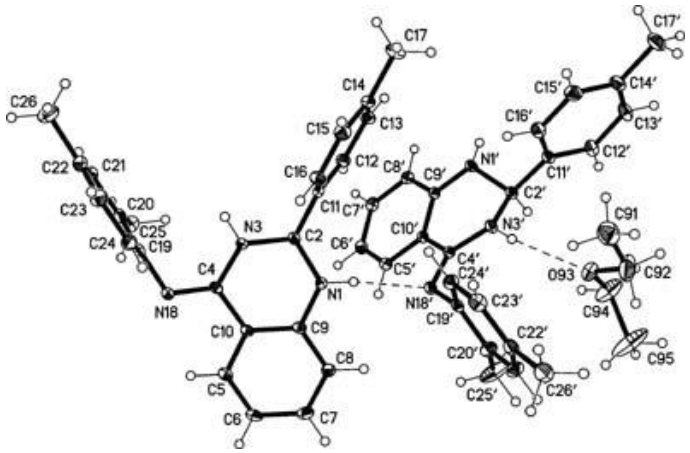


Figure 1. The asymmetric unit of compound **3e** in the crystal (including solvent). Ellipsoids represent 30% probability levels. Dashed lines indicate hydrogen bonds.

The packing of compound **3e** in the crystal lattice is as shown in Figure 2. The ^{1}H and ^{13}C NMR spectra of **4a-d** were similar to those of **3a-e** except for the second aryl group, which exhibited characteristic signals with appropriate chemical shifts. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m/z* values (see experimental section).

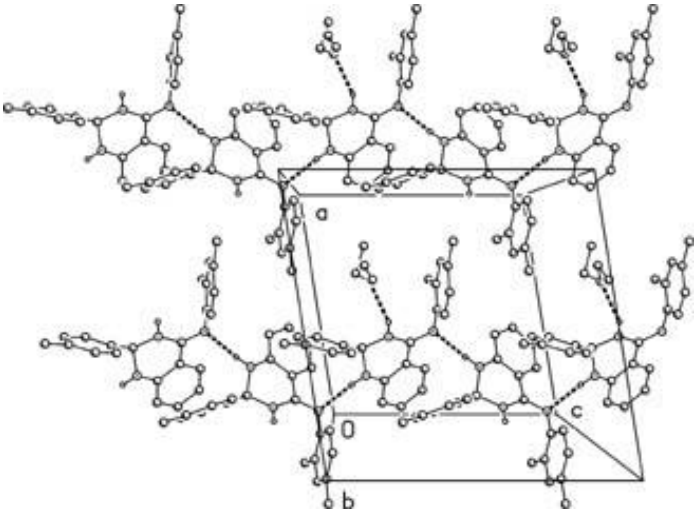
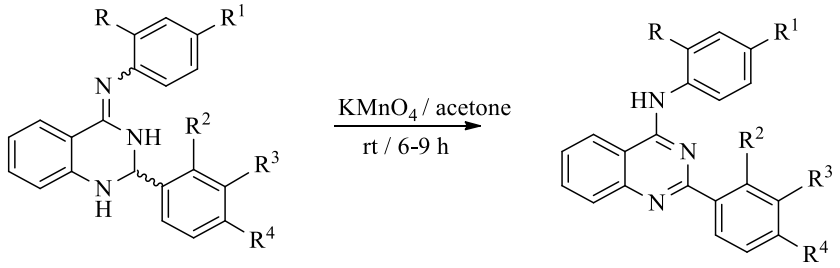


Figure 2. Packing diagram of compound **3e** in the crystal. Dashed lines indicate hydrogen bonds.

In the second part of this study the new products **3**, **4a-d** were oxidized, thus removing the chiral center. This was accomplished by treating **3**, **4a-d** with $KMnO_4$ in dry acetone (room temperature, 6-9 h; Scheme 3). The products **12**, **13a-d** were isolated in yields of 53-62% and characterized by their spectroscopic data as described in the experimental section.



3, 4a-d **12, 13a-d**

compound	**a**	**b**	**c**	**d**
3	$R=R^1=R^2=R^3=H$, $R^4=CH_3$	$R = R^2 = R^3 = H$, $R^1 = R^4 = CH_3$	$R = R^2 = R^3 = H$, $R^1 = Cl$, $R^4 = CH_3$	$R=R^2=R^3=H$, $R^1=Br$, $R^4 = CH_3$
4	$R = R^1 = R^4 = H$, $R^2=R^3=$ -CH=CH-	$R=R^4=H$, $R^1=CH_3$, $R^2=R^3=$ -CH=CH-	$R=R^4=H$, $R^1=Cl$, $R^2= R^3=$ -CH=CH-	$R=R^4=H$, $R^1 = Br$, $R^2= R^3=$ -CH=CH-

Scheme 3. Oxidation of 2,3-dihydroquinazoline derivatives **3**, **4a-d** by $KMnO_4$ in dry acetone at room temperature.

X-Ray structure determination of (3e)

Crystal data: $C_{25}H_{28}N_3O_{0.5}$, M_r = 378.50, monoclinic, $P2_1/c$, T = -173 °C, a = 11.5013(3), b = 32.8080(7), c = 11.4755(3) Å, β = 98.874(3)°, U = 4278.3 Å^3, Z = 8, F(000) = 1624, λ(Mo $K\alpha$) = 0.71073 Å, μ = 0.07 mm^{-1}, D_x = 1.175 g cm^{-3}. *Data collection:* A colourless tablet *ca*. 0.4 × 0.25

× 0.15 mm was mounted in inert oil on a glass fibre and transferred to the cold gas stream of an Oxford Diffraction Xcalibur E diffractometer. Data were recorded to 2θ 59°. *Structure refinement:* The structure was refined using SHELXL-97.[12] NH hydrogen atoms were refined freely, methyl groups as idealised rigid groups; other H were included using a riding model. The final *wR*2 (all reflections) was 0.130 for 11901 intensities and 538 parameters, with R1 ($I > 2\sigma(I)$) 0.048; *S* 1.01, max. Δρ 0.57 e $Å^{-3}$ (in solvent region).

X-ray crystallographic data (excluding structure factors) were deposited under the number CCDC-770795 and can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Conclusions

As part of our current research we have demonstrated one-pot synthesis of new (±)-*N*,2-diaryl-2,3-dihydroquinazolines through molecular iodine-catalyzed reactions from the reaction between 2-amino-*N'*-arylbenzamidines and *p*-tolualdehyde or 1-naphthaldehyde. In all cases the reaction of the two components proceeded rapidly to afford the corresponding desired products. The structure of the selected example **3e** was further confirmed by single X-ray structural analysis. The mechanism of formation of the products **3a-e** and **4a-d** is discussed. This synthetic method has the advantage to deliver good yields, no need to use hazardous and expensive catalysts and an easy workup procedure giving rise to a process with minimum waste.

Experimental Section

General. All reagents were purchased from *Alfa Aesar* and *Fluka* and were used without further purification. 2-Amino-*N'*-arylbenzamidines 1a-e were prepared according to ref[4]. Melting points were measured in capillary tubes using a Büchi 530 melting point apparatus and are uncorrected. IR spectra were measured using a Bruker Tensor 27 instrument. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded, in $CDCl_3$ and DMSO-*d6*, on a Bruker AM 400 MHz spectrometer with TMS as internal standard. The mass spectral measurements (EI, 70 eV) were performed using a Finnigan MAT 8430 spectrometer.

General procedures for preparation of compounds (3a-e) and (4a-d)

In a round-bottomed flask fitted with a magnetic stirrer a solution of **1a-e** (0.1 mmol) in dry EtOH (15 mL) was added at room temperature to a solution of aldehyde **2a**, **b** (0.1 mmol) dissolved in dry EtOH (20 mL). A solution of iodine (0.01 mmol) was added dropwise with stirring. The reaction mixture was stirred at room temperature for 1-3 h. After completion of the reaction (the reaction was followed by TLC), the main diastereoisomeric precipitate was

collected by filtration, washed and recrystallised from EtOH to afford products **3a-e** and **4a-d** in 59-71% yield.

(*Z*)-*N*-(2-*p*-Tolyl-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (3a). Yield: 48 mg, 71%; white microcrystals (from EtOH); mp 220-222 ºC; IR: ν = 3412, 3273 (NH), 1608 (C=N) cm^{-1}; ^{1}H NMR δ 2.28 (s, 3H, CH3), 4.48 (br s, 1H, NH), 5.72 (s, 1H), 6.64- 6.75 (m, 2H), 7.07-7.11 (m, 1H), 7.27-7.30 (m, 1H), 7.14-7.20 (m, 2H), 7.37 (br s, 1H, NH), 7.44-7.49 (m, 2H), 7.83-7.86 (m, 1H), 7.91 (d, 2H, *J* = 8.0 Hz), 8.13 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR δ 20.7, 69.6, 114.3, 116.4, 119.5, 120.9, 121.6, 124.1, 126.8, 128.1, 128.3, 128.5, 129.0, 131.7, 136.4, 141.5, 151.7; MS: *m/z* = 313 (M^+, 80), 298 (M^+- CH_3, 32), 274 (18), 234 (6), 221 (48), 194 (16), 171 (12), 102 (8), 91 (16), 76 (8). Anal. Calcd. for $C_{21}H_{19}N_3$: C, 80.48; H, 6.11; N, 13.41. Found: C, 80.28; H, 6.06; N, 13.28.

(*Z*)-4-Methyl-*N*-(2-*p*-tolyl-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (3b). Yield: 47 mg, 69%; white powder (from EtOH); mp 115-116 ºC; IR: ν = 3415, 3257 (NH), 1603 (C=N) cm^{-1}; ^{1}H NMR δ 2.26 (s, 3H, CH_3), 2.35 (s, 3H, CH_3) (2 CH_3 of *Z*-isomer), 2.40 and 2.31 (s, 3H, 2CH_3) (2CH_3 of *E*-isomer), 4.32 (br s, 1H, NH), 5.56 (s, 1H), 6.68 (br s, 1H, NH), 6.87-6.92 (m, 2H), 7.07 (d, 2H, *J* = 7.9 Hz), 7.19 (d, 2H, *J* = 7.8 Hz), 7.26 (d, 2H, *J* = 7.8 Hz), 7.28-7.32 (m, 2H), 7.40 (d, 2H, *J* = 7.9 Hz); ^{13}C NMR δ 20.8, 21.2, 68.4 (C-2, *Z*-isomer), 68.0 (C-2, *E*-isomer), 115.1, 116.8, 119.6, 121.4, 121.6, 123.1, 126.8, 127.4, 129.5, 130.0, 132.1, 132.2, 136.5, 139.6, 146.2, 150.5; MS: *m/z* = 327 (M^+, 40), 313 (M^+- CH_3, 100), 308 (10), 281 (4), 251 (4), 236 (56), 219 (20), 192 (16), 162 (10), 118 (12), 107 (16), 91 (28), 71 (14). Anal. Calcd. for $C_{22}H_{21}N_3$: C, 80.70; H, 6.46; N, 12.83. Found: C, 80.52; H, 6.45; N, 12.69.

(*Z*)-4-Chloro-*N*-(2-*p*-tolyl-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (3c). Yield: 46 mg, 65%; colorless powder (from EtOH); mp 126-127 ºC; IR: ν = 3378, 3213 (NH), 1609 (C=N) cm^{-1}; ^{1}H NMR (DMSO- *d6*) δ 2.38 (s, 3H, CH_3), 4.52 (br s, 1H, NH), 5.81 (s, 1H), 7.34 (d, 2H, *J* = 8.2 Hz), 7.44 (br s, 1H, NH), 7.51 (d, 2H, *J* = 8.9 Hz), 7.58-7.64 (m, 3H), 7.83-7.87 (m, 1H), 8.06 (d, 2H, *J* = 8.9 Hz), 8.37 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR (DMSO- *d6*) δ 20.9, 66.9, 113.9, 116.0, 120.4, 121.1, 123.5, 126.6, 127.9, 128.3, 128.7, 129.1, 131.5, 133.1, 135.5, 138.4, 139.9, 145.1, 150.5; MS: *m/z* = 349 (M^+ +2, 20), 347 (M^+, 48), 311 (M^+- HCl, 10), 252 (4), 219 (18), 192 (8), 172 (10), 153 (8), 128 (10), 102 (6), 91 (12), 65 (8). Anal. Calcd. for $C_{21}H_{18}ClN_3$: C, 72.51; H, 5.22; Cl, 10.19; N, 12.08. Found: C, 72.29; H, 5.18; Cl, 10.07; N, 11.87.

(*Z*)-4-Bromo-*N*-(2-*p*-tolyl-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (3d). Yield: 44 mg, 59%, colorless microcrystals (from EtOH); mp 113-114 ºC; IR: ν = 3394, 3294 (NH), 1612 (C=N) cm^{-1}; ^{1}H NMR (DMSO- *d6*) δ 2.23 (s, 3H, CH_3), 4.42 (br s, 1H, NH), 5.67 (s, 1H), 7.34-7.39 (d, 2H, *J* = 8.2 Hz), 7.44 (br s, 1H, NH), 7.51 (d, 2H, *J* = 8.7 Hz), 7.58-7.64 (m, 3H), 7.83-7.86 (m, 1H), 8.01 (d, 2H, *J* = 8.7 Hz), 8.25 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR (DMSO- *d6*) δ 21.1, 68.2, 115.0, 115.3, 116.3, 119.1, 123.4, 123.7, 126.6, 127.2, 129.4, 131.5, 132.3, 132.4, 136.2, 139.6, 146.3, 147.0, 150.5; MS: *m/z* = 393 (M^+ + 2, 78), 391 (M^+, 80), 329 (10), 314 (28), 302 (32), 274 (18), 234 (6), 221 (48), 194 (16), 171 (12), 102 (8), 91 (16), 76 (8). Anal. Calcd. for $C_{21}H_{18}BrN_3$: C, 64.30; H, 4.62; N, 10.71. Found: C, 64.09; H, 4.59; N, 10.54.

(*Z*)-2,4-Dimethyl-*N*-(2-*p*-tolyl-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (3e). Yield: 41 mg, 59%, pale yellow powder (from EtOH); mp 120-121 ºC; IR: ν = 3406, 3312 (NH), 1605 (C=N) cm^{-1}; ^{1}H NMR δ 2.15 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.30 (s, 1H, NH), 5.52 (s, 1H), 6.63-6.67 (dd, 1 H, *J* = 0.9, 8.1 Hz), 6.84-6.89 (m, 2H), 6.95 (d, 1H, *J* = 0.9 Hz), 7.17 (d, 2H, *J* = 7.8 Hz), 7.26-7.32 (m, 2H), 7.36 (d, 1H, *J* = 8.0 Hz), 7.77 (d, 2H, *J* = 7.8 Hz), 8.25 (s, 1H); ^{13}C NMR δ 17.7, 20.7, 21.2, 68.2, 115.0, 119.6, 121.0, 127.3, 127.4, 128.4, 129.0, 129.2, 129.5, 129.7, 129.8, 131.4, 131.8, 131.9, 132.6, 139.7, 145.9, 149.2; MS: *m/z* = 341 (M^+, 24), 339 (32), 308 (M^+- 2 CH_3, 6), 279 (4), 264 (10), 236 (8), 223 (100), 207 (28), 193 (6), 165 (8), 149 (16), 132 (44), 119 (22), 103 (10), 91 (26), 72 (16). Anal. Calcd. for $C_{23}H_{23}N_3$: C, 80.90; H, 6.79; N, 12.31. Found: C, 80.69; H, 6.73; N, 12.17.

(*Z*)-*N*-(2-(Naphthalen-1-yl)-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (4a). Yield: 40 mg, 67%, yellow powder (from EtOH); mp 212-214 ºC; IR: ν = 3361, 3240 (NH), 1624 (C=N) cm^{-1}; ^{1}H NMR δ 4.50 (br s, 1H, NH), 6.13 (s, 1H), 7.29 (br s, 1H, NH), 7.35-7.42 (m, 4H), 7.47-7.55 (m, 3H), 7.74-7.81 (m, 4H), 7.94 (d, 2H, *J* = 6.6 Hz), 8.06 (d, 2H, *J* = 6.2 Hz), 8.75 (s, 1H); ^{13}C NMR δ 68.0, 102.3, 113.3, 117.2, 120.4, 121.1, 123.8, 125.2, 125.6, 126.3, 126.6, 127.2, 128.9, 129.0, 129.1, 129.8, 131.3, 132.8, 134.1, 137.0, 138.6, 150.6; MS: *m/z* = 349 (M^+, 44), 347 (80), 346 (100), 305 (8), 270 (24), 255 (16), 234 (10), 230 (28), 220 (8), 192 (4), 172 (18), 155 (12), 141 (4), 127 (24), 118 (16), 93 (12), 77 (24). Anal. Calcd. for $C_{24}H_{19}N_3$: C, 82.49; H, 5.48; N, 12.03. Found: C, 82.31; H, 5.47; N, 11.88.

(*Z*)-4-Methyl-*N*-(2-(naphthalen-1-yl)-2,3-dihydroquinazolin-4(1*H*)-ylidene)-aniline (4b). Yield: 37 mg, 60%, yellow microcrystals (from EtOH); mp 120-121 ºC; IR: ν = 3380, 3239 (NH), 1626 (C=N) cm^{-1}; ^{1}H NMR δ 2.89 (s, 3H, CH_3), 4.77 (br s, 1H, NH), 6.29 (s, 1H), 6.66-6.73 (m, 1H), 6.97-7.01 (m, 1H), 7.07 (br s, 1H, NH), 7.32-7.36 (m, 1H), 7.45-7.52 (m, 2H), 7.57-7.62 (m, 2H), 7.77 (d, 2H, *J* = 7.7 Hz), 7.87 (s, 1H), 7.95 (d, 2H, *J* = 7.9 Hz), 8.12-8.19 (m, 3H); ^{13}C NMR δ 20.8, 63.3, 101.7, 115.4, 119.5, 121.7, 125.4, 125.7, 125.8, 126.1, 126.2, 126.5, 127.1, 128.6, 129.0, 129.2, 129.5, 129.9, 130.0, 132.3, 135.4, 143.6, 152.0; MS: *m/z* = 363 (M^+, 72), 360 (100), 344 (12), 319 (4), 270 (20), 236 (32), 209 (12), 192 (8), 172 (12), 141 (8), 127 (16), 107 (14), 77 (8). Anal. Calcd. for $C_{25}H_{21}N_3$: C, 82.61; H, 5.82; N, 11.56. Found: C, 82.48; H, 5.81; N, 11.43.

(*Z*)-4-Chloro-*N*-(2-(naphthalen-1-yl)-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (4c). Yield: 39 mg, 61%, pale yellow solid (from EtOH); mp 240-242 ºC; IR: ν = 3307, 3247 (NH), 1608 (C=N) cm^{-1}; ^{1}H NMR (DMSO-*d6*) δ 4.25 (br s, 1H, NH), 6.21 (s, 1H), 7.27 (br s, 1H, NH), 7.60-7.69 (m, 4H), 7.77-7.87 (m, 4H), 7.89-7.95 (m, 3H), 8.19 (d, 2H, *J* = 8.2 Hz), 8.80 (d, 2H, *J* = 8.3 Hz); ^{13}C NMR (DMSO- *d6*) δ 65.71, 101.5, 115.01, 116.8, 119.3, 122.9, 123.4, 124.9, 125.7, 126.2, 126.5, 128.7, 129.8, 131.1, 131.8, 132.2, 132.4, 133.5, 134.3, 147.2, 151.4; MS: *m/z* = 385 (M^+ + 2, 32), 383 (M^+, 80), 380 (100), 344 (36), 317 (4), 270 (42), 255 (20), 228 (8), 190 (16), 172 (28), 153 (10), 127 (12), 111 (4), 75 (8). Anal. Calcd. for $C_{24}H_{18}ClN_3$: C, 75.09; H, 4.73; N, 10.95. Found: C, 74.87; H, 4.66; N, 10.77.

(*Z*)-4-Bromo-*N*-(2-(naphthalen-1-yl)-2,3-dihydroquinazolin-4(1*H*)-ylidene)aniline (4d). Yield: 36 mg, 54%, pale yellow solid (from EtOH); mp 160-161 ºC; IR: ν = 3379, 3253 (NH),

1610 (C=N) cm^{-1}; ^1H NMR δ 4.54 (br s, 1H, NH), 6.17 (s, 1H), 7.19-7.28 (m, 4H), 7.31 (br s, 1H, NH), 7.35-7.43 (m, 4H), 7.70-7.79 (m, 3H), 7.93 (d, 2H, *J* = 8.3 Hz), 8.31 (d, 2H, *J* = 8.3 Hz); ^{13}C NMR δ 66.7, 103.2, 115.0, 116.8, 119.2, 121.6, 122.9, 123.5, 124.9, 125.8, 126.1, 126.3, 128.7, 129.8, 131.1, 131.9, 132.1, 132.4, 134.0, 146.7, 150.6, 152.2; MS: *m/z* = 429 (M^+ + 2, 80), 427 (M^+, 76), 346 (12), 344 (20), 314 (8), 302 (60), 300 (100), 275 (40), 257 (60), 230 (8), 220 (20), 194 (14), 173 (58), 153 (12), 127 (24), 92 (18). Anal. Calcd. for $C_{24}H_{18}BrN_3$: C, 67.30; H, 4.24; N, 9.81. Found: C, 67.12; H, 4.19; N, 9.68.

General procedures for preparation of compounds (12, 13a-d)

To a solution of **3**, **4a-d** (0.1 mmol) dissolved in dry acetone (15 mL), a solution of $KMnO_4$ (0.11 mmol) was added drop by drop with constant stirring. The reaction mixture was stirred at room temperature for 6-9 h. After completion of the reaction, it was quenched with a saturated solution of sodium sulfite. After stirring for 1 h, the product was extracted three times with CH_2Cl_2 (20 mL), the collected organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude products **12**, **13a-d** was subjected to column chromatography over silica gel using CH_2Cl_2 as eluent to give the pure desired products in 53-62% yield.

***N*-Phenyl-2-*p*-tolylquinazolin-4-amine (12a).** Yield: 60 mg, 60%, pale yellow powder; mp 193-194 ºC; IR: ν = 3327 (NH), 1615, 1602 (C=N) cm^{-1}; ^1H NMR δ 2.34 (s, 3H, CH_3), 7.05-7.11 (m, 2H), 7.21 (br s, 1H, NH), 7.19-7.24 (m, 2H), 7.36-7.43 (m, 3H), 7.67-7.74 (m, 2H), 7.84 (d, 2H, *J* = 8.3 Hz), 8.35 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR δ 24.7, 113.8, 116.0, 120.8, 121.4, 123.7, 125.6, 126.2, 127.2, 128.3, 128.7, 129.0, 129.2, 129.5, 132.6, 140.2, 150.9, 157.4, 160.2; MS: *m/z* = 311 (M^+, 100), 281 (4), 265 (10), 249 (12), 234 (8), 219 (14), 192 (8), 179 (6), 155 (8), 125 (4), 119 (10), 97 (8), 91 (12). Anal. Calcd. for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.77; H, 5.52; N, 13.35.

***N*,2-di-*p*-Tolylquinazolin-4-amine (12b).** Yield: 55 mg, 55%, pale yellow powder; mp 105-106 ºC; IR: ν = 3258 (NH), 1621, 1601 (C=N) cm^{-1}; ^1H NMR δ 2.27 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 7.18 (d, 2H, *J* = 8.2 Hz), 7.34 (d, 2H, *J* = 7.8 Hz), 7.51 (br s, 1H, NH), 7.67-7.76 (m, 4H), 7.80 (d, 2H, *J* = 7.9 Hz), 8.40 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR δ 21.4, 22.1, 113.5, 120.1, 122.3, 125.8, 126.3, 128.3, 128.6, 128.7, 128.9, 129.1, 129.5, 132.7, 135.7, 137.2, 140.5, 151.8, 157.6, 160.4; MS: *m/z* = 325 (M^+, 80), 324 (M^+-1, 100), 309 (M^+- CH_3, 4), 248 (10), 235 (14), 219 (12), 192 (10), 162 (12), 121 (16), 102 (6), 91 (8), 71 (4). Anal. Calcd. for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91. Found: C, 81.07; H, 5.87; N, 12.79.

***N*-(4-Chlorophenyl)-2-*p*-tolylquinazolin-4-amine (12c).** Yield: 57 mg, 57%, yellowish-white powder; mp 133-134 ºC; IR: ν = 3440 (NH), 1615, 1599 (C=N) cm^{-1}; ^1H NMR δ 2.27 (s, 3H, CH_3), 7.17 (d, 2H, *J* = 8.1 Hz), 7.22 (d, 2H, *J* = 8.8 Hz), 7.63 (br s, 1H, NH), 7.69 (d, 2H, *J* = 8.8 Hz), 7.80-7.89 (m, 4H), 8.27 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR δ 21.4, 113.5, 120.1, 122.3, 125.8, 128.3, 128.6, 128.7, 128.9, 129.1, 129.4, 132.7, 135.7, 137.2, 140.5, 150.9, 156.9, 160.1; MS: *m/z* = 347 (M^+ + 2, 24), 345 (M^+, 68), 344 (M^+-1, 100), 308 (8), 268 (4), 228 (4), 219 (20), 192 (10), 153 (6), 119 (6), 102 (8), 91 (81), 65 (8). Anal. Calcd. for $C_{21}H_{16}ClN_3$: C, 72.93; H, 4.66; Cl, 10.25; N, 12.15. Found: C, 72.71; H, 4.65; Cl, 10.11; N, 11.99.

***N*-(4-Bromophenyl)-2-*p*-tolylquinazolin-4-amine (12d).** Yield: 53 mg, 53%, colourless powder; mp 119-120 ºC; IR: ν = 3372 (NH), 1612, 1600 (C=N) cm^{-1}; ^{1}H NMR δ 2.39 (s, 3H, CH_3), 7.31 (d, 2H, *J* = 8.1 Hz), 7.39 (br s, 1H, NH), 7.45-7.54 (m, 4H), 7.55 (d, 2H, *J* = 8.8 Hz), 7.80 (d, 2H, *J* = 8.8 Hz), 8.40 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR δ 24.8, 116.9, 120.1, 122.7, 126.0, 126.7, 127.3, 128.4, 129.2, 129.9, 131.9, 132.9, 135.6, 140.6, 149.7, 154.8, 160.0; MS: *m/z* = 391 (M^+ + 2, 42), 389 (M^+, 38), 281 (4), 265 (10), 249 (12), 234 (8), 219 (14), 192 (8), 179 (6), 155 (8), 125 (4), 119 (10), 97 (8), 91 (12). Anal. Calcd. for $C_{21}H_{16}BrN_3$: C, 64.63; H, 4.13; N, 10.77. Found: C, 64.39; H, 4.12; N, 10.65.

2-(Naphthalen-1-yl)-*N*-phenylquinazolin-4-amine (13a). Yield: 53 mg, 54%, yellowish-brown solid; mp 192-194 ºC; IR: ν = 3294 (NH), 1617, 1603 (C=N) cm^{-1}; ^{1}H NMR δ 7.39 (br s, 1H, NH), 7.42 (m, 2H), 7.50-7.55 (m, 2H), 7.63-7.69 (m, 2H), 7.72-7.79 (m, 3H), 7.81-7.84 (m, 1H), 7.87-7.95 (m, 3H), 8.05-8.09 (m, 1H), 8.45-8.49 (m, 2H); ^{13}C NMR δ 115.5, 119.6, 121.3, 125.4, 125.8, 126.1, 126.2, 126.5, 127.1, 128.6, 129.0, 129.2, 129.5, 129.9, 130.1, 131.2, 132.3, 135.4, 143.6, 152.0, 158.2, 160.5; MS: *m/z* = 347 (M^+, 46), 270 (24), 255 (12), 234 (18), 230 (8), 220 (10), 192 (6), 172 (18), 155 (12), 141 (4), 127 (24), 118 (16), 93 (12), 77 (24). Anal. Calcd. for $C_{24}H_{17}N_3$: C, 82.97; H, 4.93; N, 12.10. Found: C, 82.79; H, 4.90; N, 11.97.

2-(Naphthalen-1-yl)-*N*-*p*-tolylquinazolin-4-amine (13b). Yield: 56 mg, 57%, yellow microcrystals; mp 133-134 ºC; IR: ν = 3277 (NH), 1612, 1600 (C=N) cm^{-1}; ^{1}H NMR δ 2.29 (s, 3H, CH_3), 7.39 (br s, 1H, NH), 7.42 (d, 2H, *J* = 8.0 Hz), 7.50-7.57 (m, 2H), 7.63-7.69 (m, 2H), 7.74-7.79 (m, 2H), 7.82 (d, 2H, *J* = 8.1 Hz), 7.87-7.91 (m, 1H), 8.05-8.11 (m, 2H), 8.45-8.53 (m, 2H); ^{13}C NMR δ 20.9, 115.5, 119.5, 121.3, 125.4, 125.8, 126.1, 126.2, 126.5, 127.1, 128.6, 129.0, 129.2, 129.5, 129.9, 130.1, 132.3, 135.4, 143.6, 152.0, 158.2, 160.5; MS: *m/z* = 361 (M^+, 88), 345 (32), 319 (10), 270 (12), 236 (22), 209 (12), 192 (8), 172 (12), 141 (8), 127 (16), 107 (14), 77 (8). Anal. Calcd. for $C_{25}H_{19}N_3$: C, 83.08; H, 5.30; N, 11.63. Found: C, 82.89; H, 5.28; N, 11.49.

***N*-(4-Chlorophenyl)-2-(naphthalen-1-yl)quinazolin-4-amine (13c).** Yield: 54 mg, 55%, yellow powder; mp 185-186 ºC; IR: ν = 3258 (NH), 1619, 1601 (C=N) cm^{-1}; ^{1}H NMR δ 7.30 (d, 2H, *J* = 8.9 Hz), 7.41-7.46 (m, 2H), 7.50 (br s, 1H, NH), 7.52-7.59 (m, 3H), 7.81 (d, 2H, *J* = 8.9 Hz), 7.84-7.92 (m, 3H), 8.05-8.08 (dd, 1H, *J* = 0.7, 8.4 Hz), 8.11-8.15 (dd, 1H, *J* = 1.3, 7.2 Hz), 8.73-8.77 (m, 1H); ^{13}C NMR δ 113.3, 122.1, 122.0, 125.2, 125.7, 126.3, 126.5, 126.6, 128.4, 128.9, 129.0, 129.2, 129.5, 130.0, 131.3, 133.1, 134.2, 136.8, 137.2, 150.8, 156.9, 162.6; MS: *m/z* = 383 (M^+ + 2, 52), 381 (M^+, 100), 344 (M^+- Cl, 24), 270 (32), 255 (10), 228 (6), 190 (12), 172 (20), 153 (8), 127 (12), 111 (4), 75 (8). Anal. Calcd. for $C_{24}H_{16}ClN_3$: C, 75.49; H, 4.22; Cl, 9.28; N, 11.00. Found: C, 75.22; H, 4.19; Cl, 9.13; N, 10.82.

***N*-(4-Bromophenyl)-2-(naphthalen-1-yl)quinazolin-4-amine (13d).** Yield: 62 mg, 62%, yellow powder; mp = 169-171 ºC; IR: ν = 3305 (NH), 1614, 1603 (C=N) cm^{-1}; ^{1}H NMR δ 7.30 (d, 2H, *J* = 8.9 Hz), 7.41-7.46 (m, 2H), 7.50 (br s, 1H, NH), 7.81 (d, 2H, *J* = 8.9 Hz), 7.52-7.56 (m, 3H), 7.84-7.89 (m, 3H), 8.04-8.07 (dd, 1H, *J* = 0.7, 8.4 Hz), 8.11-8.15 (dd, 1H, *J* = 1.3, 7.2 Hz), 8.73-8.78 (m, 1H); ^{13}C NMR δ 113.3, 122.0, 122.1, 125.2, 125.5, 126.4, 126.5, 126.6, 128.4, 128.9, 129.1, 129.3, 129.5, 130.0, 131.3, 133.0, 134.1, 136.7, 136.9, 151.6, 155.8, 161.7;

MS: *m/z* = 427 (M^+ + 2, 64), 425 (M+, 60), 345 (M^+- Br, 18), 270 (12), 255 (18), 228 (16), 190 (4), 172 (6), 153 (8), 127 (12), 111 (4), 75 (8). Anal. Calcd. for $C_{24}H_{16}BrN_3$: C, 67.62; H, 3.78; N, 9.86. Found: C, 67.37; H, 3.77; N, 9.70.

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