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UV-light induced domino type reactions: synthesis and photophysical properties of unreported nitrogen ring junction quinazolines†

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An expedient method for the synthesis of 5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazolines by UV light has been developed. Our aim was to synthesize various α, β-unsaturated carbonyl compounds and to further react them with different amines in DMF, in the presence of potassium hydroxide as base, which leads to cyclization and the aromatized products in a single step using UV irradiation at 254 nm. We have performed the reaction with various other bases and solvents that lead to the desired product with a lower yield. The synthesized ring junction compounds have been characterized by suitable spectroscopic techniques. The fluorescence emission spectra of the synthesized compounds were recorded in DMF.

Introduction

Quinazoline derivatives are nitrogen-containing heterocyclic compounds which have a universal impact due to their biological and pharmaceutical activities.[1] Researchers have already determined many therapeutic activities of quinazoline derivatives, including anti-cancer,[2–4] anti-inflammation,[5,6] anti-bacterial,[7–9] analgesia,[10] anti-virus,[11] anti-cytotoxin,[12] anti-spasmodic,[13] anti-tuberculosis,[14] anti-oxidation,[15] antimalarial,[16] anti-hypertension,[17] anti-obesity,[18] anti-psychotic,[19] anti-diabetes,[20] *etc.*, along with the quinazoline core motif. We have also found several triazolo pyrimidine core structures with highly important medical activities for neurological disorders, anti-cancer, anti-bacterial, anti-viral cases, and also with cytotoxic activities. Over past decades, researchers have been focusing on fused heterocyclic compounds with a nitrogen ring junction due to their biologically potent properties.[21–23] Unfortunately, the majority of ring junction systems do not occur naturally, but they have more importance than just a theoretical viewpoint. Replacement of a carbon atom and its attached hydrogen atoms by heteroatoms like nitrogen, sulphur or oxygen, either in five or six-membered rings, leads to a wide variety of heterocycles. Their pharmacological activities also vary hugely. Some of the ring junction nitrogen analogues have been used as dyes as well. Recent literature has been enriched with an overview on the syntheses of various heterocyclic compounds using non-conventional energy sources like microwave irradiation, ultraviolet light,[24,25] ultrasonic waves, *etc.* To bring novelty to the existing work, our interest was mainly to focus on the synthesis of triazoloquinazoline ring junction nitrogen compounds using UV-irradiation *via* a domino type reaction.[26] The cascade reaction or domino reaction or tandem reaction has drawn special focus in organic transformations. Despite their biological activity, there are limited reports of fluorescence studies of triazoloquinazoline fused systems. This gap was identified by our research group and so we planned the synthesis of a series of triazoloquinazolines and to subject them to fluorescence studies.

Results and discussion

We have also reported a series of short reviews on arylation *via* transition metal free conditions.[27] The background literature revealed that Scheme 1 was closely related to our present research experiments. Drizin *et al.* (2002), synthesized dihydropyrolopyrimidine fused rings by a one pot methodology with excellent yields.[28] The reactions were carried out in the absence of a catalyst. In 2005, Shikhaliev *et al.* demonstrated the neat reaction to synthesise dihydrotriazolo pyrimidine derivatives with excellent yields.[29]

In 2008, Majid *et al.* synthesised dihydrotriazolo pyrimidine derivatives *via* a one pot multi component methodology using a tungsten catalyst.[30]

Desenko *et al.*, in 1991, synthesized a set of tetrahydro triazoloquinazolines from chalcones and 2*H*-[1,2,4]triazol-3-ylamine in DMF.[31] Many literature reports record either the synthesis of ring junction nitrogen compounds without aromatization or two step procedures were necessary to get the aromatized ring junction nitrogen compound.[32–34] To aromatize

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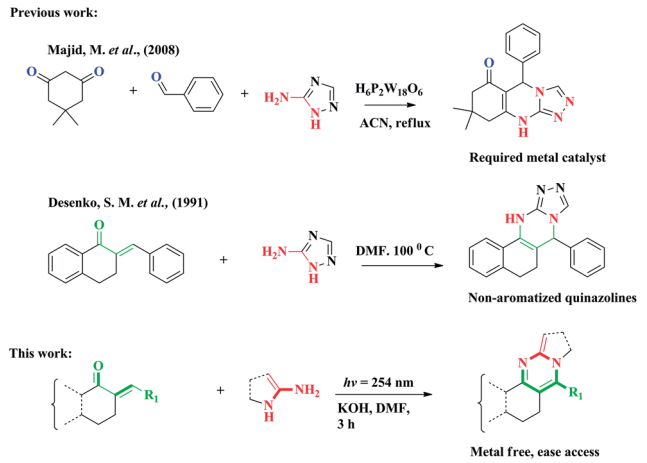


Scheme 1 Synthesis of nitrogen ring junction quinazoline derivatives by various methodologies.

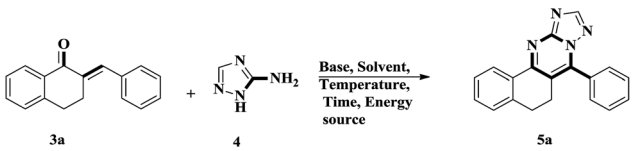
the compound, DDQ[35]/toluene, PhCl/*p*-chloranil[36] or CAN/acetone[37] were used. However, these methodologies require a longer time for the completion of the reaction and provide a lower yield. These gaps prompted us towards the synthesis of a couple of 5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazolines.

Our research methodology involves the reaction between a series of α,β-unsaturated carbonyl compounds and 2*H*-[1,2,4]-triazol-3-ylamine in the presence of potassium hydroxide as a base in DMF under UV-irradiation (Scheme 1). The reaction mixture was irradiated for 3 h at 254 nm and led to the cyclization, followed by the aromatized products, in a single step with good to excellent yields. We have synthesised an array of 5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline derivatives.

The synthesized triazoloquinazolines were characterized by spectral analyses. The synthesised compounds were subjected to fluorescence studies and the quantum yields of fluorescent-active compounds were calculated. During fine tuning of the reaction conditions, no product conversion was observed with ethanol or with neat conditions (entry 1 and 2, Table 1). A moderate yield was observed when using strong bases like ^{t}BuOK, NaOH and KOH.

After performing the reaction under different conditions, we found that the KOH/DMF combination with 1 h at room temperature in the presence of UV irradiation at 254 nm provided the best yield (entry 21). The reaction time also played an important role in increasing the yield of the product (Table 1). With optimized conditions in hand, the scope of the methodology was examined. We synthesized 22 α,β-unsaturated carbonyl compounds and known compounds were confirmed by their melting points and ^{1}H NMR data matching with reported data. The compounds **5a** and **5n** formed with 92% product (isolated yield). From the above result, the substitution on the

Table 1 Fine tuning the optimal reaction conditions for the compound **5a**[a]

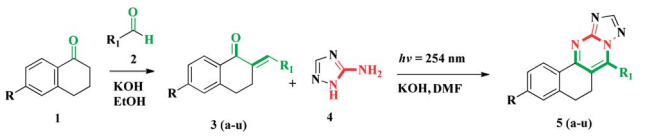


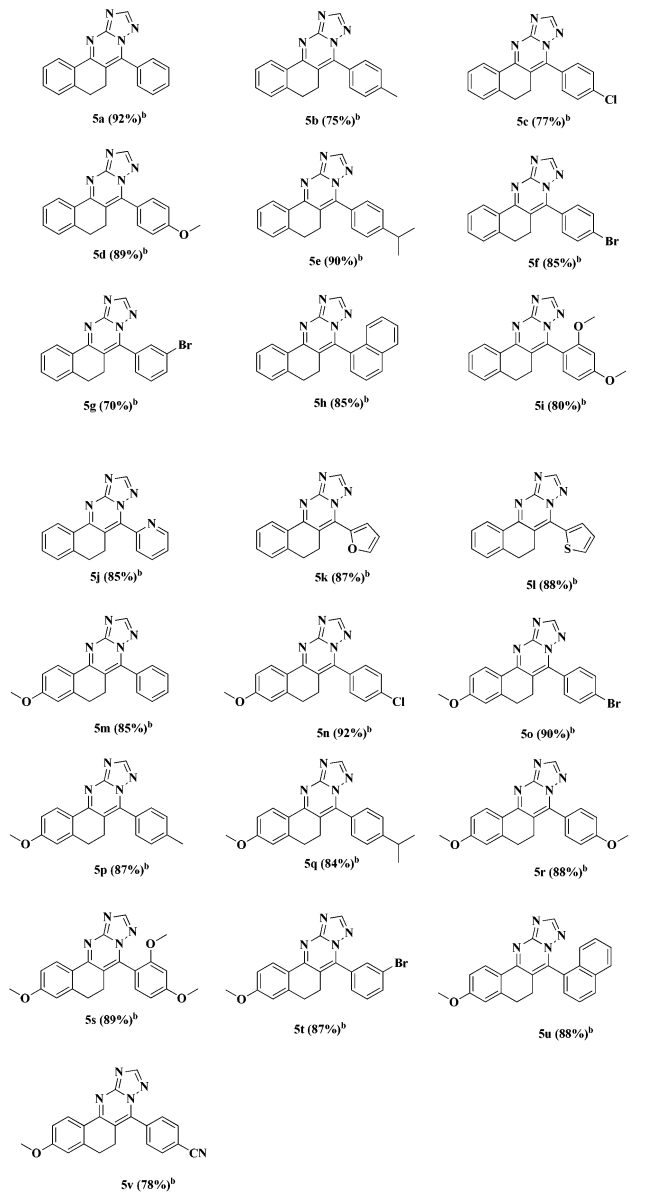
3a 4 5a

Entry	Base	Solvent	Temp. (°C)	Source	Time (h)	Yield[b] (%)
1	—	—	100	Δ	16	NR
2	—	EtOH	80	Δ	16	NR
3	Triethylamine	EtOH	80	Δ	16	NR
4	Piperidine	EtOH	80	Δ	16	NR
5	NaOMe	MeOH	80	Δ	16	Trace
6	NaOEt	EtOH	80	Δ	16	75
7	NaO^{t}Bu	*t*-BuOH	100	Δ	16	40
8	KO^{t}Bu	*t*-BuOH	100	Δ	16	30
9	NaOH	EtOH	80	Δ	16	50
10	KOH	EtOH	80	Δ	16	56
11	KOH	DMSO	80	Δ	3	45
12	KOH	DMSO	80	Δ	5	25
13	KOH	THF	80	Δ	3	16
14	KOH	ACN	80	Δ	3	16
15	KOH	DMF	80	Δ	3	87
16	KOH	DMF	60	Δ	5	67
17	KOH	DMF	100	Δ	3	50
18	KOH	DMF	80	MW (100 W)	0.5	60
19	KOH	DMF	RT	US	3	55
20	**KOH**	**DMF**	**RT**	**UV (254 nm)**	**1**	**92**
21	KOH	DMF	RT	UV (312 nm)	3	67
22	KOH	DMF	RT	UV (365 nm)	3	55

[a] Where Δ = conventional heating, MW = microwave, UV = ultraviolet irradiation, US = ultra sonication, NR = no reaction and RT = room temperature. The optimal conditions are shown by bold letters. [b] Isolated yield.

Table 2 Synthesis of 5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline derivatives[a]





[a] Reactions were carried out with 1.0 equivalent of **3**, **4** and 1.2 equivalent of KOH in 10 mL DMF for 3 h. [b] Isolated yields.

α,β-unsaturated carbonyl compounds were not playing any important role in the product formation. The synthesized α,β-unsaturated carbonyl compounds were reacted with 2*H*-[1,2,4] triazol-3-ylamine in the presence of KOH/DMF to afford the product with good to excellent yield (Table 2).

On the basis of the above fine-tuned reaction conditions, we utilized the same methodology for different amines and α,β-unsaturated carbonyls to provide compounds with fair to good yields. The synthesized compounds 2-benzylidene cyclohexanone **6e** and 2-benzylidene cyclopentanone **6d** failed to afford the required products under the same conditions (Table 3).

The compound **5a** was also synthesized by a one pot multi component reaction. The conditions involved equimolar amounts of the three reactants with a KOH/DMF combination under UV irradiation to afford the product with an isolated yield of 20% (Scheme 2). In the multistep reaction, the compounds **3a** and **5a** were synthesized with 94% yield[38] and 92% isolated yield, respectively. Compared with the above conditions, the Multi Component Reaction (MCR) gave 20% product (isolated yield).

The fluorescence emission spectra of the synthesized compounds **5a–v** were recorded in DMF (10^{-5} M). Among these compounds **5d**, **5e**, **5h**, **5k**, **5l**, **5m**, **5o**, **5q**, **5u** and **5v** showed fluorescence properties (Fig. 1).

We calculated the quantum yield (Φ) of the fluorescence active compounds. The Φ was calculated using the formula,

$$\Phi = (\Phi_R \times I_S \times OD_R \times \eta_s)/(I_R \times OD_S \times \eta_R)$$

where Φ_R = quantum yield of the reference, I_S and I_R = integral area of the sample and the reference, respectively, OD_S and OD_R = excited absorbance of the sample and the reference, respectively, η_s and η_R = refractive index of the sample solvent and the reference solvent, respectively. We used tryptophan[40–43] as a standard for calculating the quantum yield (Table 4). For the standard we used water as a solvent and for the synthesised compounds we used DMF.

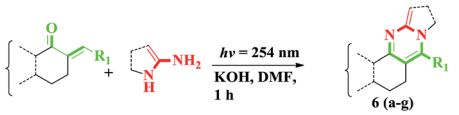
Conclusions

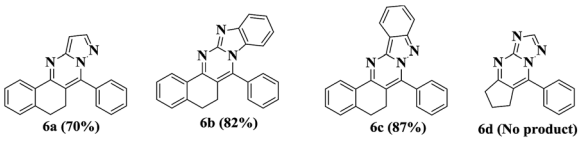
In conclusion, we have developed an efficient and easy protocol for the synthesis of triazoloquinazoline fused ring systems through a domino type transformation. Moreover, this method offers shorter reaction times, remarkable yields and transition metal free reaction conditions. Some of the derivatives showed fluorescence activity and we have calculated the quantum yield for these fluorescence active compounds. In the future, we plan to investigate the biological activities of the synthesized compounds.

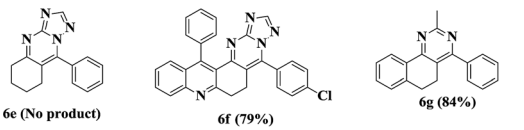
Experimental section

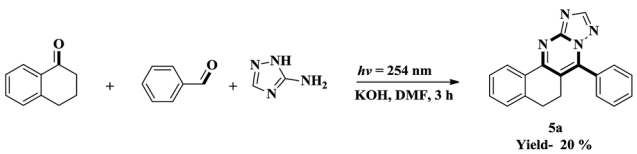
All commercially available reagents were used without further purification and the reactions were monitored by TLC. The ^{1}H and ^{13}C NMR spectra were obtained using a Bruker Avance 400 MHz spectrometer in $CDCl_3$ solvent with TMS as an internal standard. Chemical shift values (δ) were expressed in parts per million (ppm). Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet. The melting points were measured on an Elchem Microprocessor based DT apparatus using open capillary tubes and are uncorrected. The mass spectra were obtained by high resolution mass spectrometry.

Table 3 Scope for various amines and α,β-unsaturated carbonyls









Scheme 2 Synthesis of 7-phenyl-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline *via* a multi component one pot methodology.

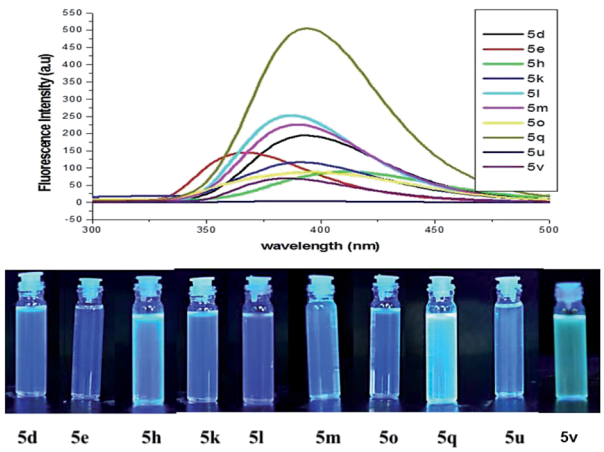


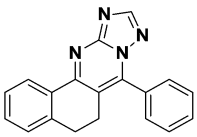
Fig. 1 Fluorescence emission spectra of the synthesised compounds.

The UV-Visible spectra were obtained on a UV-2550, Shimadzu Corporation, Kyoto, Japan. The fluorescence spectra were obtained on a Hitachi F-7000 FL spectrophotometer. Column chromatography was performed using 60–120 mesh silica gel. UV-irradiation was carried out in a Heber multi-wavelength multi-lamp photo reactor (Model HML-LP88).

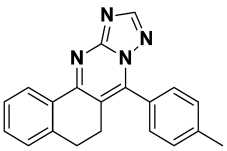
General procedure for the synthesis of 5,6-dihydrobenzo[*h*]-[1,2,4]triazolo[5,1-*b*]quinazolines [5a–i & 6a–f]

A mixture of the α,β-unsaturated carbonyl compound (1 mmol) and amine (1 mmol) were mixed in a 50 mL quartz UV reaction vial containing 10 mL of dimethylformamide and potassium hydroxide (1.2 mmol) was added at room temperature. The mixture was irradiated under UV at 254 nm (8 lamps) with constant stirring. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was poured into crushed ice and the solid was filtered. The solid was dissolved in EtOAc and mixed with water and the organic layer was separated. The separated organic layer was dried over sodium sulphate and the solvent was evaporated. The crude product was further purified by column chromatography to afford the product as a solid.

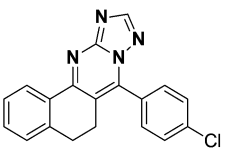
Characterization data for the compounds [5a–i & 6a–f]



7-Phenyl-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5a). Brown solid; isolated yield – 92%; mp: 201–203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62–8.59 (m, 1H), 8.39 (s, 1H), 7.62–7.61 (m, 5H), 7.46 (t, J = 4.4 Hz, 2H), 7.29 (d, J = 4.0 Hz, 1H), 2.95 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 27.9, 117.8, 127.3, 127.7, 127.9, 128.9, 129.0, 129.5, 130.7, 131.7, 132.7, 139.5, 144.5, 155.7, 158.5; HRMS: *m*/*z* calcd for $C_{19}H_{14}N_4$ 298.1218 found 298.1210.



7-(*p*-Tolyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5b). Off-white solid; isolated yield – 75%; mp: 240–242 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61–8.59 (m, 1H), 8.38 (s, 1H), 7.51–7.42 (m, 6H), 7.29–7.26 (m, 1H), 3.00–2.91 (m, 4H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 24.7, 27.9, 117.7, 126.0, 127.2, 127.6, 127.9, 129.4, 129.6, 131.6, 132.8, 139.6, 141.1, 144.7, 154.9, 155.6, 158.5; HRMS: *m*/*z* calcd for $C_{20}H_{16}N_4$ 312.1375 found 312.1370.

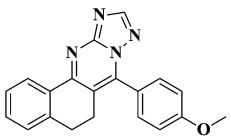


7-(4-Chlorophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5c). Off-white solid; isolated yield – 77%; mp: 266–268 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60–8.58 (m, 1H), 8.38 (s, 1H), 7.62–7.55 (m, 4H), 7.47–7.43 (m, 2H), 7.29–7.28 (m, 1H), 2.95 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 26.7, 116.9, 126.2, 126.2, 126.7, 126.9, 128.3, 130.0, 130.8, 131.5, 136.0, 138.4, 142.2, 153.8, 154.7, 157.5; HRMS: *m*/*z* calcd for $C_{19}H_{13}ClN_4$ 332.0829 found 332.0820.

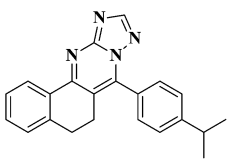
Table 4 Photophysical data for the fluorescence active compounds[a]

Entry	λ_{max} (abs, nm)	λ_{max} (em, nm)	Stokes shift (nm)	OD	*I*	*Φ*
Tryptophan[39]	280	355	75	0.384	158 517	0.130
5d	271	392	121	0.823	15 887	0.006
	253 (Sh)	392	139	0.671	15 887	0.008
5e	259	365	106	0.948	9773	0.003
	277 (Sh)	365	88	0.547	9773	0.006
5h	265	415	150	1.137	9029	0.002
	275 (Sh)	415	140	0.712	9029	0.004
5k	264 (Sh)	391	127	1.117	11 363	0.003
	277	391	114	0.724	11 363	0.005
5l	276 (Sh)	386	110	0.679	18 578	0.009
	264	386	122	0.430	18 578	0.014
5m	274 (Sh)	423	149	0.592	17 844	0.010
	261	423	162	0.302	17 844	0.020
5o	266	430	164	0.745	9546	0.004
5q	267	428	161	0.983	37 482	0.013
5u	270 (Sh)	450	180	0.707	18 747	0.008
	246	450	204	0.638	18 747	0.010
5v	260	384	124	1.178	5181	0.001
	251 (Sh)	384	133	0.575	5181	0.002

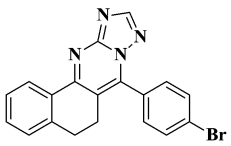
[a] Sh = shoulder; abs = absorbance; em = emission; OD = excited absorbance; *I* = integral area; *Φ* = quantum yield.



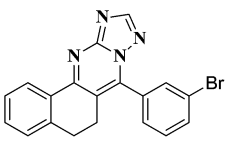
7-(4-Methoxyphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5d). Brown solid; isolated yield – 89%; mp: 204–206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60–8.58 (m, 1H), 8.38 (s, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.46–7.44 (m, 2H), 7.29–7.26 (m, 1H), 7.13 (d, J = 8.8 Hz, 2H), 3.92 (s, 3H), 3.02–2.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 28.0, 55.5, 114.3, 117.6, 120.9, 127.2, 127.6, 127.8, 131.3, 131.6, 132.8, 139.5, 144.5, 154.9, 155.6, 158.5, 161.3; HRMS: *m*/*z* calcd for $C_{20}H_{16}N_4O$ 328.1324 found 328.1320.



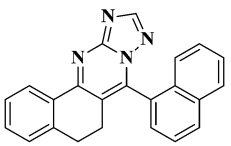
7-(4-Isopropylphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5e). Off-white solid; isolated yield – 90%; mp: 190–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61–8.58 (m, 1H), 8.40 (s, 1H), 7.56–7.44 (m, 6H), 7.28–7.26 (m, 1H), 3.07–2.91 (m, 5H), 1.34 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 24.1, 26.9, 33.4, 117.7, 126.1, 126.3, 126.4, 127.3, 128.2, 129.9, 131.5, 132.4, 140.0, 144.5, 150.9, 154.2, 155.3, 157.4; HRMS: *m*/*z* calcd for $C_{22}H_{20}N_4$ 340.1688 found 340.1680.



7-(4-Bromophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5f). Off-white solid; isolated yield – 85%; mp: 218–220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61–8.58 (m, 1H), 8.39 (s, 1H), 7.78–7.76 (m, 2H), 7.51–7.45 (m, 4H), 7.29–7.26 (m, 1H), 2.96 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 27.8, 117.9, 125.4, 127.3, 127.7, 127.9, 129.5, 131.2, 131.8, 132.3, 132.6, 139.4, 143.3, 154.9, 155.7, 158.6; HRMS: *m*/*z* calcd for $C_{19}H_{13}BrN_4$ 376.0324 found 376.0320.

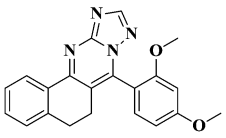


7-(4-Bromophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5g). Off-white solid; isolated yield – 70%; mp: 208–210 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60–8.58 (m, 1H), 8.39 (s, 1H), 7.76–7.74 (m, 2H), 7.56–7.43 (m, 4H), 7.29–7.26 (m, 1H), 2.95 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 27.8, 118.1, 123.0, 127.3, 127.7, 127.9, 128.2, 130.5, 130.8, 131.9, 132.4, 132.5, 133.8, 139.5, 142.8, 155.8, 158.6; HRMS: *m*/*z* calcd for $C_{19}H_{13}BrN_4$ 376.0324 found 376.0320.

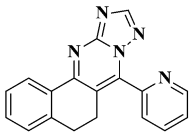


7-(Naphthalen-1-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]-quinazoline (5h). Yellow solid; isolated yield – 85%; mp: 203–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69–8.66 (m, 1H), 8.34 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.72–7.43 (m, 6H), 7.29–7.26 (m, 2H), 2.92–2.86 (m, 2H), 2.80–2.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 27.7, 119.5, 124.1,

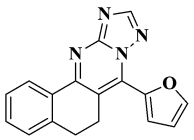
125.4, 126.7, 126.9, 127.3, 127.6, 127.7, 128.0, 129.0, 130.3, 131.2, 131.8, 132.6, 133.7, 139.7, 155.0, 155.9, 158.3; HRMS: *m*/*z* calcd for $C_{23}H_{16}N_4$ 348.1375 found 348.1370.



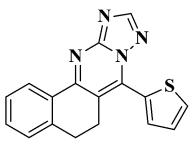
7-(2,4-Dimethoxyphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5i). Yellow solid; isolated yield – 80%; mp: 194–196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62–8.60 (m, 1H), 8.37 (s, 1H), 7.47–7.42 (m, 2H), 7.28–7.26 (m, 1H), 7.13–6.95 (m, 3H), 3.82 (s, 3H), 3.72 (s, 3H), 2.96–2.83 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 27.7, 55.8, 56.2, 112.9, 115.9, 117.2, 118.6, 119.2, 127.2, 127.6, 127.9, 131.5, 132.8, 139.8, 142.0, 151.2, 153.6, 154.9, 155.5, 158.0; HRMS: *m*/*z* calcd for $C_{21}H_{18}N_4O_2$ 358.1430 found 358.1400.



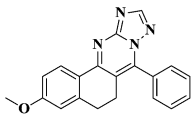
7-(Pyridin-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5j). Off-white solid; isolated yield – 85%; mp: 230–232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J = 4.8 Hz, 1H), 8.62–8.59 (m, 1H), 8.41 (s, 1H), 8.02–7.98 (m, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.55–7.49 (m, 3H), 7.29–7.26 (m, 1H), 3.05–2.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 27.6, 118.8, 125.0, 126.1, 127.3, 127.6, 127.9, 131.8, 132.5, 136.9, 139.7, 142.1, 148.5, 150.2, 154.9, 155.8, 159.0; HRMS: *m*/*z* calcd for $C_{18}H_{13}N_5$ 299.1171 found 299.1170.



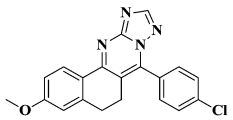
7-(Furan-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5k). Off-white solid; isolated yield – 87%; mp: 196–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (t, J = 6.8 Hz, 1H), 8.49 (s, 1H), 8.04 (d, J = 3.6 Hz, 1H), 7.80 (s, 1H), 7.45 (t, J = 4.4 Hz, 2H), 7.31–7.26 (m, 1H), 6.78 (d, J = 2 Hz, 1H), 3.50 (t, J = 6.8 Hz, 2H), 3.02 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 27.7, 112.4, 116.9, 120.7, 127.3, 127.6, 127.6, 131.5, 132.8, 139.5, 145.3, 155.4; HRMS: *m*/*z* calcd for $C_{17}H_{12}N_4O$ 288.1011 found 288.1000.



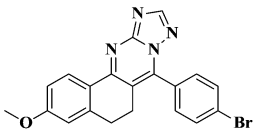
7-(Thiophen-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5l). Off-white solid; isolated yield – 88%; mp: 226–228 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57–8.56 (m, 1H), 8.45 (s, 1H), 7.79–7.77 (m, 1H), 7.67–7.66 (m, 1H), 7.48–7.42 (m, 2H), 7.32–7.27 (m, 2H), 3.23–3.20 (m, 2H), 2.97 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 27.9, 118.4, 127.1, 127.3, 127.7, 128.2, 130.7, 131.6, 132.8, 132.9, 138.8, 139.2, 155.4, 158.3; HRMS: *m*/*z* calcd for $C_{17}H_{12}N_4S$ 304.0783 found 304.0780.



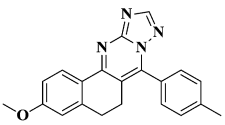
3-Methoxy-7-phenyl-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5m). Off-white solid; isolated yield – 85%; mp: 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 8.4 Hz, 1H), 8.34 (s, 1H), 7.65–7.58 (m, 5H), 6.99–6.96 (m, 1H), 6.77 (d, J = 2.4 Hz, 1H), 3.89 (s, 3H), 2.96–2.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 28.2, 55.4, 112.9, 113.4, 117.2, 125.7, 128.9, 129.1, 129.3, 129.5, 130.6, 141.7, 144.2, 154.9, 155.4, 158.5, 162.5; HRMS: *m*/*z* calcd for $C_{20}H_{16}N_4O$ 328.1324 found 328.1320.



7-(4-Chlorophenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5n). Off-white solid; isolated yield – 92%; mp: 210–212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.8 Hz, 1H), 8.34 (s, 1H), 7.61–7.54 (m, 4H), 6.99–6.96 (m, 1H), 6.78 (d, J = 2.4 Hz, 1H), 3.89 (s, 3H), 2.92 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 28.1, 55.4, 112.9, 113.5, 117.2, 125.5, 127.4, 129.3, 129.4, 131.0, 137.0, 141.6, 142.9, 155.4, 158.5, 162.6; HRMS: *m*/*z* calcd for $C_{20}H_{15}ClN_4O$ 362.0934 found 362.0930.

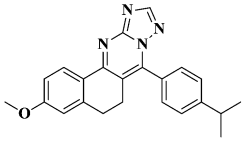


7-(4-Bromophenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5o). Off-white solid; isolated yield – 90%; mp: 206–208 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.8 Hz, 1H), 8.34 (s, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 6.99–6.96 (m, 1H), 6.78 (d, J = 2.0 Hz, 1H), 3.89 (s, 3H), 2.92 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 28.1, 55.4, 112.9, 113.5, 117.2, 125.5, 127.9, 129.4, 131.2, 132.2, 141.6, 142.9, 155.5, 158.5, 162.6; HRMS: *m*/*z* calcd for $C_{20}H_{15}BrN_4O$ 406.0429 found 406.0420.

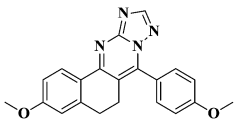


3-Methoxy-7-(*p*-tolyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5p). Off-white solid; isolated yield – 87%; mp: 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 8.8 Hz, 1H), 8.33 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 6.99–6.96 (m, 1H), 6.78 (d, J = 2.4 Hz, 1H), 3.89 (s, 3H), 2.96–2.90 (m, 4H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 24.7, 28.2, 55.4, 112.9, 113.3, 117.0, 125.7, 126.1, 129.3, 129.4, 129.5, 141.0,

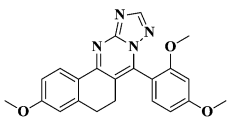
141.7, 144.4, 155.4, 162.5; HRMS: *m*/*z* calcd for $C_{21}H_{18}N_4O$ 342.1481 found 342.1480.



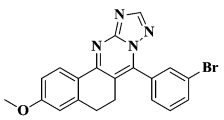
7-(4-Isopropylphenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4]-triazolo[5,1-*b*]quinazoline (5q). Off-white solid; isolated yield – 84%; mp: 208–210 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 8.8 Hz, 1H), 8.33 (s, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 6.99–6.96 (m, 1H), 6.76 (d, J = 2.4 Hz, 1H), 3.95 (s, 3H), 3.07–2.88 (m, 5H), 1.33 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 24.8, 28.3, 34.2, 55.4, 112.9, 113.3, 117.1, 125.8, 126.4, 127.0, 129.3, 129.6, 141.7, 144.4, 151.6, 155.0, 155.4, 158.4, 162.4; HRMS: *m*/*z* calcd for $C_{23}H_{22}N_4O$ 370.1794 found 370.1790.



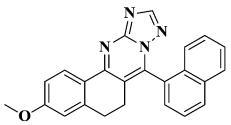
3-Methoxy-7-(4-methoxyphenyl)-5,6-dihydrobenzo[*h*][1,2,4]-triazolo[5,1-*b*]quinazoline (5r). Yellow solid; isolated yield – 88%; mp: 196–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.8 Hz, 1H), 8.34 (s, 1H), 7.56 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 6.98–6.95 (m, 1H), 6.77 (d, J = 2.0 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 2.90–2.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 28.3, 55.4, 55.4, 112.9, 113.3, 114.3, 117.0, 121.0, 125.8, 129.3, 131.3, 141.6, 144.2, 155.0, 155.3, 158.4, 161.2, 162.4; HRMS: *m*/*z* calcd for $C_{21}H_{18}N_4O_2$ 358.1430 found 358.1400.



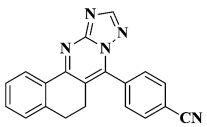
7-(2,4-Dimethoxyphenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4]-triazolo[5,1-*b*]quinazoline (5s). Yellow solid; isolated yield – 89%; mp: 190–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.8 Hz, 1H), 8.34 (s, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 7.00–6.97 (m, 1H), 6.79–6.67 (m, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.77 (s, 3H), 2.98–2.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 28.2, 55.4, 55.6, 55.6, 99.1, 105.2, 110.6, 112.9, 113.2, 118.7, 125.9, 129.2, 131.5, 141.9, 141.9, 155.1, 157.9, 158.4, 162.3, 163.0; HRMS: *m*/*z* calcd for $C_{22}H_{20}N_4O_3$ 388.1535 found 388.1530.



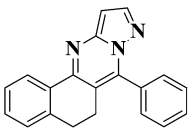
7-(3-Bromophenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5t). Off-white solid; isolated yield – 87%; mp: 210–212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.4 Hz, 1H), 8.35 (s, 1H), 7.75–7.55 (m, 2H), 7.55–7.48 (m, 2H), 6.99–6.96 (m, 1H), 6.78 (d, J = 2.4 Hz, 1H), 3.89 (s, 3H), 2.92 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 28.1, 55.4, 112.9, 113.5, 117.4, 122.9, 125.5, 128.2, 129.4, 130.5, 130.9, 132.4, 133.7, 141.6, 142.4, 154.9, 155.5, 158.5, 162.6; HRMS: *m*/*z* calcd for $C_{20}H_{15}BrN_4O$ 406.0429 found 407.0501.



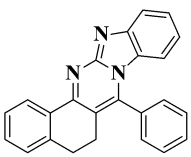
3-Methoxy-7-(naphthalen-1-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5u). Off-white solid; isolated yield – 88%; mp: 256–258 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 8.8 Hz, 1H), 8.29 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.69–7.01 (m, 6H), 6.76 (d, J = 2.0 Hz, 1H), 3.89 (s, 3H), 2.88–2.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 28.1, 55.4, 113.0, 113.5, 118.8, 124.1, 125.4, 125.6, 126.8, 127.5, 127.7, 129.0, 129.4, 130.4, 131.1, 133.7, 141.9, 143.3, 155.6, 158.2, 162.6; HRMS: *m*/*z* calcd for $C_{24}H_{18}N_4O$ 378.1481 found 378.1480.



4-(5,6-Dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazolin-7-yl)-benzonitrile (5v). Off-white solid; isolated yield – 78%; mp: 250–252 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (t, J = 6.8 Hz, 1H), 8.38 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.48–7.44 (m, 2H), 7.30–7.27 (m, 1H), 2.98–2.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 27.7, 114.7, 117.8, 118.1, 127.3, 127.8, 128.0, 130.6, 132.0, 132.3, 132.6, 133.3, 139.3, 142.1, 154.8, 155.8, 158.7; HRMS: *m*/*z* calcd for $C_{20}H_{13}N_5$ 323.3507 found 323.5409.

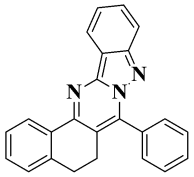


7-Phenyl-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]quinazoline (6a). Brown solid; isolated yield – 70%; mp: 220–222 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 6.4 Hz, 1H), 8.02 (s, 1H), 7.59–7.55 (m, 5H), 7.43–7.37 (m, 2H), 7.25 (d, J = 4 Hz, 1H), 6.73 (s, 1H), 2.87–2.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 28.3, 96.6, 115.4, 126.2, 127.4, 127.9, 128.8, 129.6, 130.1, 130.2, 130.6, 133.5, 139.3, 143.1, 144.5, 148.4, 153.0; HRMS: *m*/*z* calcd for $C_{20}H_{15}N_3$ 297.1266 found 297.1260.

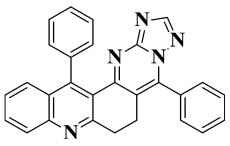


7-Phenyl-5,6-dihydrobenzo[*h*]benzo[4,5]imidazo[2,1-*b*]quinazoline (6b). Yellow solid; isolated yield – 82%; mp: 270–272 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70–8.68 (m, 1H), 7.92–7.73 (m, 1H), 7.72–7.69 (m, 3H), 7.51–7.23 (m, 6H), 6.94 (t, J = 7.6 Hz, 1H),

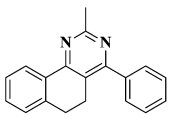
6.18 (d, J = 8.4 Hz, 1H), 2.95–2.91 (m, 2H), 2.78–2.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 28.1, 113.9, 114.8, 119.9, 120.8, 125.4, 127.3, 127.5, 127.9, 127.9, 128.6, 129.9, 130.7, 131.4, 131.5, 133.1, 140.0, 144.6, 145.2, 151.4, 158.2; HRMS: m/z calcd for $C_{24}H_{17}N_3$ 347.1422 found 347.1420.



7-Phenyl-5,6-dihydrobenzo[*h*]indazolo[3,2-*b*]quinazoline (6c). Yellow solid; isolated yield – 87%; mp: 290–292 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 7.6 Hz, 1H), 8.40 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.64–7.73 (m, 8H), 7.28–7.25 (m, 2H), 2.95 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 28.1, 114.0, 116.5, 119.4, 120.3, 120.9, 126.1, 127.5, 127.9, 129.0, 129.2, 129.8, 130.2, 130.3, 130.4, 133.6, 138.8, 142.1, 143.5, 149.6, 151.1; HRMS: m/z calcd for $C_{24}H_{17}N_3$ 347.1422 found 347.1420.



5,13-Diphenyl-6,7-dihydro-[1,2,4]triazolo[1′,5′:1,2]pyrimido-[4,5-*a*]acridine (6f). Brown solid; isolated yield – 79%; mp: 342–344 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.67–7.45 (m, 9H), 7.34 (bs, 2H), 3.33 (t, J = 6.4 Hz, 2H), 3.09 (t, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 33.5, 119.8, 126.6, 127.0, 127.8, 128.0, 128.1, 128.2, 128.6, 129.3, 129.4, 131.1, 131.2, 137.2, 137.3, 143.0, 150.0, 156.0, 159.5; HRMS: m/z calcd for $C_{28}H_{19}N_5$ 425.1640 found 425.1620.



2-Methyl-4-phenyl-5,6-dihydrobenzo[*h*]quinazoline (6g). Off-white semi-solid; isolated yield – 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40–8.39 (m, 1H), 7.60–7.49 (m, 2H), 7.47–7.39 (m, 5H), 7.26–7.25 (m, 1H), 3.00–2.81 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 26.2, 27.8, 122.4, 125.8, 127.3, 127.7, 128.4, 128.9, 129.1, 130.8, 133.1, 138.1, 139.1, 160.0, 164.3, 165.7.

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