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UV-Light induced Domino type reactions: Synthesis and photo physical properties of unreported nitrogen ring junction quinazolines

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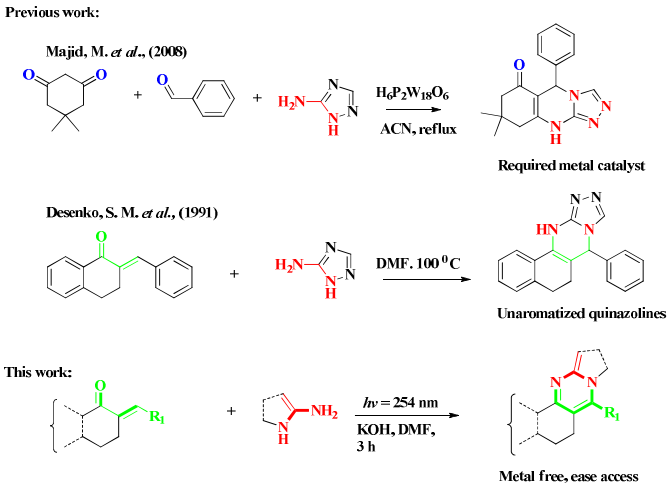
An expedient method for the synthesis of 5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazolines have been developed by UV light medium. Our aim is to synthesize various *α, β* - unsaturated carbonyl compounds and further it was reacted with different amines in the presence of potassium hydroxide as the base in DMF which leads to the cyclization followed by aromatized products in single step *via* UV irradiation at 254 nm. We have employed the reaction with various other bases and solvents that leads to the desired product with 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 universal concerns 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 which shows major medically important activities in neurological disorder, anti-cancer, anti-bacterial, anti-viral and cytotoxic activities. Over past decades, the researchers have been focusing on fused heterocyclic compounds with nitrogen ring junction due to its biological potent properties. [21-23] Unfortunately, majority of the ring junction systems do not occur naturally, but they had much importance than theoretical viewpoints. Replacement of carbon atom with its attached hydrogen atom by heteroatoms like nitrogen, sulphur or oxygen either in five or six-membered rings leads to a wide variety of heterocycles. Its pharmacological activities also vary with huge parameter. Some of the ring junction nitrogen analogue has been used as dyes as well. Recent literatures were enriched with an overview on the synthesis of various heterocyclic compounds using non-conventional energy sources like microwave, ultraviolet [24,25], ultrasonic waves, etc., to bring the novelty from the existing work, our interest was mainly to focus on the synthesis of triazoloquinazolines ring junction nitrogen compounds using UV-irradiation *via* Domino type reaction.[26] The Cascade reaction or Domino reaction or Tandem reaction had drawn special focuses in organic transformations. Despite of their biological activity, there was limited report on the fluorescence studies of triazoloquinazoline fused systems. This gap was identified from our research group and further planned for the synthesis of triazoloquinazolines series and to subject them for its fluorescence studies.

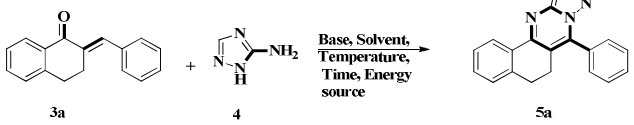
Results and Discussion

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



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

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



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	Traces
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
21	**KOH**	**DMF**	**RT**	**UV (254 nm)**	**1**	**92**
22	KOH	DMF	RT	UV (312 nm)	3	67
23	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 optimized condition was mentioned by bold letters. [b]Isolated yield.

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

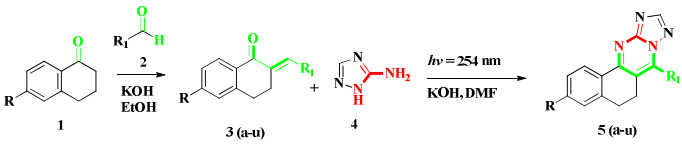
Desenko *et al.*, in 1991, synthesized a set of tetrahydro triazolo quinazolines from chalcones and 2*H*-[1,2,4]triazol-3-ylamine in DMF.[31] Many literature report states that, the synthesis of ring junction nitrogen compound without aromatization and two step procedures was followed to get the aromatized ring junction nitrogen compound [32-34]. To aromatize the compound DDQ[35]/Toluene or PhCl/*p*-chloranil [36] or CAN/acetone [37] were used. However, these methodologies required longer time for the completion of reaction, provided with lower yield. These gaps prompted us towards the synthesis 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 presence of potassium hydroxide as a base in DMF under UV-irradiation **(Scheme 1)**.The reaction mixture was irradiated for 3h at 254 nm lead to the cyclization followed by aromatized products in a single step with good to excellent yields ratio. We have synthesised array of 5,6-dihydrobenzo [*h*] [1,2,4] triazolo [5,1-*b*] quinazoline derivatives.

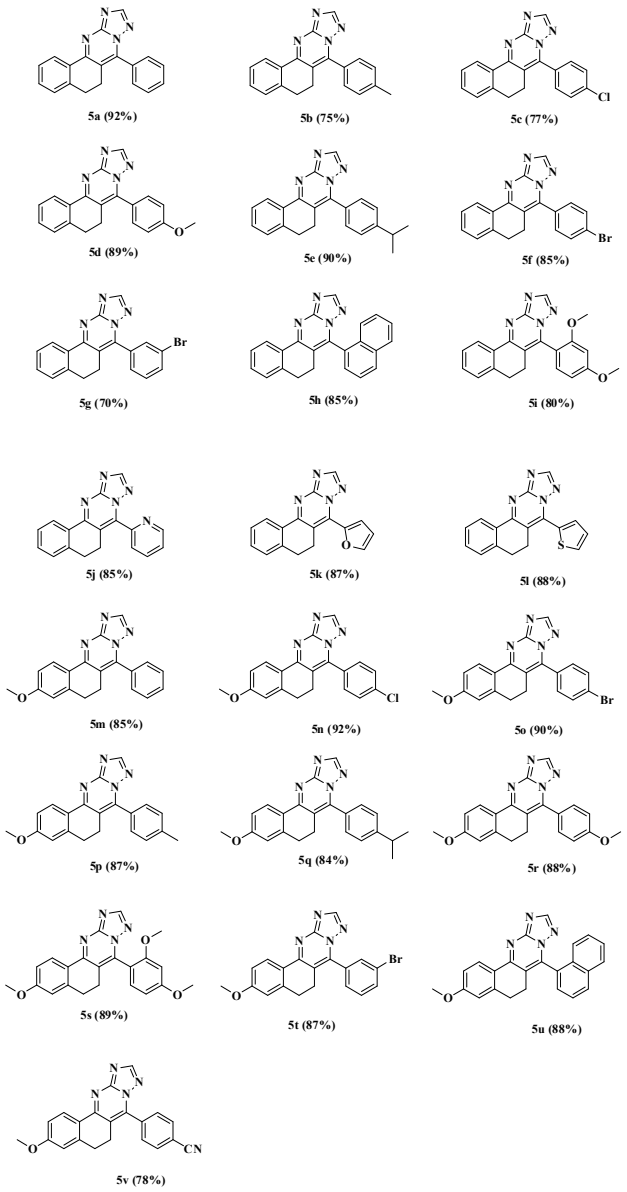
The synthesized triazoloquinazolines were characterized by their respective spectral analysis. The synthesised compounds were subjected for fluorescent studies and quantum yield of fluorescent active compounds were calculated. During fine tuning of the reaction conditions, no product conversion was observed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

After performing a different reaction conditions, we have found KOH/DMF combination with 1h at room temperature in the presence of UV irradiation at 254 nm provided then good yield among others (entry 21). The reaction time also played an important role to increase the yield of the product **(Table 1).** With optimized condition in hand, the scope of the methodology was examined. We have synthesized 22 *α, β*-unsaturated carbonyl compounds and known compounds were confirmed by its melting points and ^{1}H NMR data matching with reported data. The compound 5a and 5n formed with 92% product (isolated yield). From the above result, the substitution on α, β-unsaturated carbonyl compounds were not playing any important role in the product formation. The synthesized α, β- unsaturated carbonyl compounds are reacted with 2*H*-[1, 2, 4] triazol-3-ylamine in presence of KOH/DMF afford the product with good to excellent yield **(Table 2).**

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



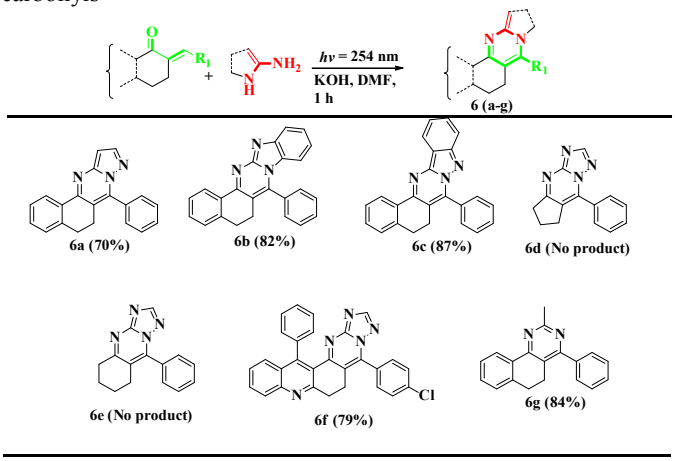
1 3 (a-u) 4 5 (a-u)

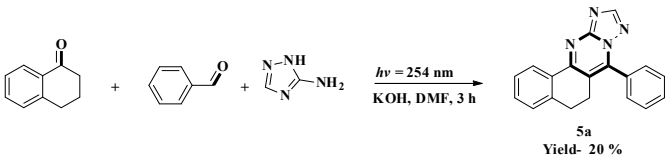


[a]Reactions were carried out with 1.0 equivalent of **3**, **4** and 1.2 equivalent of KOH in 10 volume of DMF for 3h .[b]Isolated yields.

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

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* multi component one pot methodology.

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

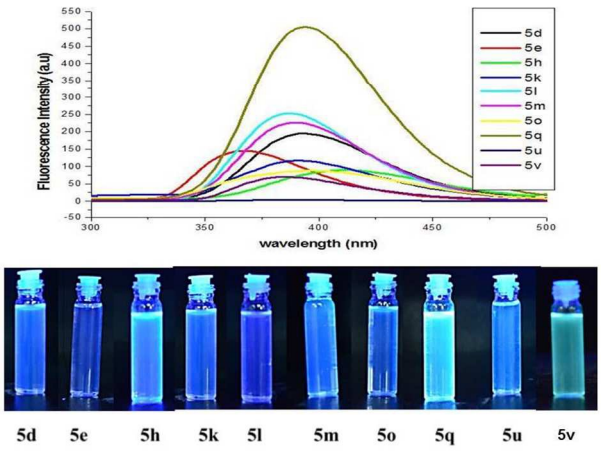


Fig 1. Fluorescence emission spectra of the synthesised compounds.

The fluorescence emission spectra of the synthesized compounds 5(a-u) 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)**.

Table 4. Photo physical data for fluorescence active compounds

Entry	λmax (abs, nm)	λmax (em, nm)	Stokes shift (nm)	OD	I	Φ
Tryptophan[39]	280	355	75	0.384	158517	0.130
5d	271	392	121	0.823	15887	0.006
	253 (sh)	392	139	0.671	15887	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	11363	0.003
	277	391	114	0.724	11363	0.005
5l	276 (sh)	386	110	0.679	18578	0.009
	264	386	122	0.430	18578	0.014
5m	274 (sh)	423	149	0.592	17844	0.010
	261	423	162	0.302	17844	0.020
5o	266	430	164	0.745	9546	0.004
5q	267	428	161	0.983	37482	0.013
5u	270 (sh)	450	180	0.707	18747	0.008
	246	450	204	0.638	18747	0.010
5v	260	384	124	1.178	5181	0.001
	251 (sh)	384	133	0.575	5181	0.002

Sh = shoulder; abs = absorbance; em = emission; OD = excited absorbance; I = integral area; Φ = emission of quantum yield

We have calculated the emission of quantum yield (Φ) of the fluorescence active compounds. The Φ_R was calculated by using below formula,

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

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

Conclusion

In conclusion, we have delivered an efficient and easy protocol for the synthesis of triazolquinazolines fused ring system through Domino type transformation. Moreover, this method offers less reaction time, remarkable yields and transition metal free reaction conditions. Some of the derivatives showed fluorescent activities and we have calculated emission of quantum yield for the above fluorescence active compounds. In future we have planned for the biological activities of synthesized compounds.

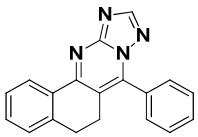
Experimental section

All commercially available reagents were used without further purification and the reactions were monitored by TLC. The ^1H and ^{13}C NMR were obtained using a Bruker Avance 400 Mz 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 Elchem Microprocessor based DT apparatus using an open capillary tubes and are uncorrected. The mass spectra were obtained by high resolution mass spectrometer. The UV-Visible spectrum was obtained on UV-2550, Shimadzu Corporation, Kyoto, Japan. The fluorescence spectra were obtained on Hitachi F-7000 FL spectrophotometer. The column chromatography was performed using 60-120 mesh silica gel. The UV-irradiation was carried out in Heber multiwavelength multilamp photo reactor (Model HML-LP88)

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

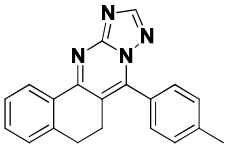
A mixture of *α, β*- unsaturated carbonyl compound (1 mmol) and amine (1 mmol) were mixed in 50 mL quartz UV reaction vial containing 10 mL of dimethylformamide and added potassium hydroxide (1.2 mmol) at room temperature. The mixture was irradiated under UV at 254 nm (8 lamps) with constant stirring.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

Characterization data for the compounds [5(a-i) & 6(a-f)]



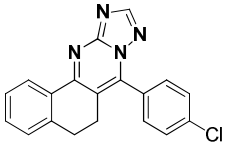
7-phenyl-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5a)

Brown solid; Isolated yield - **92** %; mp: 201-203 °C; ^1H 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.



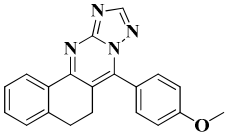
7-(p-tolyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5b)

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.



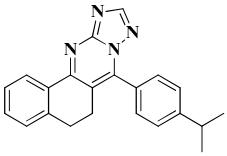
7-(4-chlorophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5c)

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



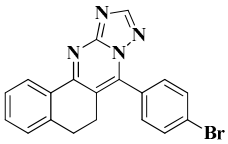
7-(4-methoxyphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5d)

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.



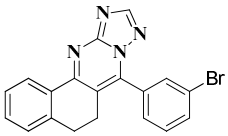
7-(4-isopropylphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5e)

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.



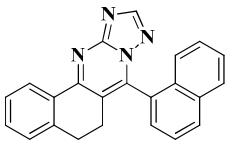
7-(4-bromophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5f)

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.



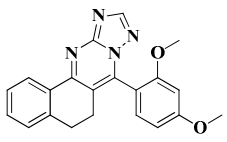
7-(4-bromophenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5g)

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.



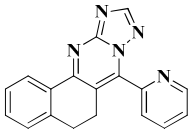
7-(naphthalen-1-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5h)

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.



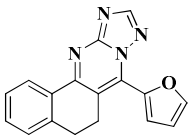
7-(2,4-dimethoxyphenyl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5i)

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.



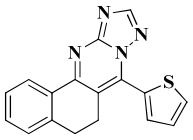
7-(pyridin-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5j)

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.



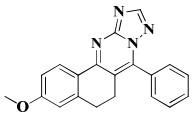
7-(furan-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5k)

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* = 2Hz, 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.



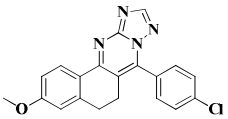
7-(thiophen-2-yl)-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*] quinazoline (5l)

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.



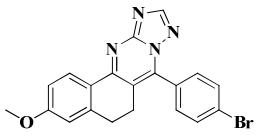
3-methoxy-7-phenyl-5,6-dihydrobenzo[*h*][1,2,4]triazolo[5,1-*b*]quinazoline (5m)

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.



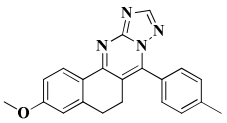
7-(4-chlorophenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4] triazolo [5,1-*b*] quinazoline (5n)

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* = 2.4Hz, 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)

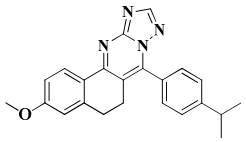
Off-White solid; Isolated yield - 90 %; mp: 206-208 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.8 Hz, 1H), 8.34 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 6.99-6.96 (m, 1H), 6.78 (d, *J* = 2.0Hz, 1H), 3.89 (s, 3H), 2.92 (bs, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 28.1, 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)

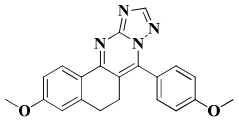
Off-White solid; Isolated yield - 87 %; mp: 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 8.8 Hz, 1H), 8.33 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.99-6.96 (m, 1H), 6.78 (d, *J* = 2.4Hz, 1H), 3.89 (s, 3H), 2.96-2.900 (m, 4H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 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.



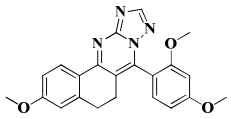
7-(4-isopropylphenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4] triazolo[5,1-*b*]quinazoline (5q)

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.



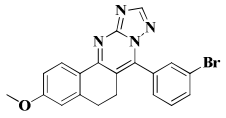
3-methoxy-7-(4-methoxyphenyl)-5,6-dihydrobenzo[*h*] [1,2,4] triazolo[5,1-*b*]quinazoline (5r)

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* = 2.0Hz, 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.



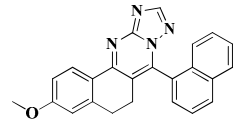
7-(2,4-dimethoxyphenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4] triazolo[5,1-*b*]quinazoline (5s)

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.



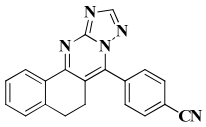
7-(3-bromophenyl)-3-methoxy-5,6-dihydrobenzo[*h*][1,2,4] triazolo[5,1-*b*]quinazoline (5t)

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.



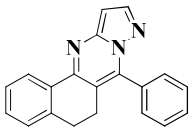
3-methoxy-7-(naphthalen-1-yl)-5,6-dihydrobenzo[*h*][1,2,4] triazolo[5,1-*b*]quinazoline (5u)

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* = 2.0Hz, 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.



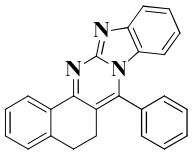
4-(5,6-dihydrobenzo[h][1,2,4]triazolo[5,1-b]quinazolin-7-yl)benzonitrile (5v)

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.



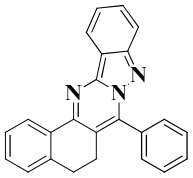
7-phenyl-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]quinazoline (6a)

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* = 4Hz, 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.



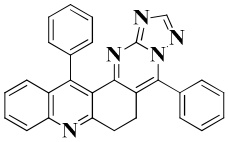
7-phenyl-5,6-dihydrobenzo[*h*]benzo[4,5]imidazo[2,1-*b*] quinazoline (6b)

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), 6.942 (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.



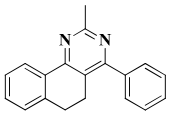
7-phenyl-5,6-dihydrobenzo[*h*]indazolo[3,2-*b*]quinazoline (6c)

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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Notes and references

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