Synthesis of New Diversely Linked Biquinoline Derivatives by Multicomponent Imino-Diels–Alder Cycloaddition and Intramolecular Friedel–Crafts Cyclization

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Abstract: New and efficient routes for diversely linked 2,6′-, 2,7′-, 2,2′-, or 2,8′-biquinoline derivatives are reported. These routes are based on the powerful methodologies of imino-Diels–Alder cycloaddition reactions and intramolecular Friedel–Crafts cyclization reactions.

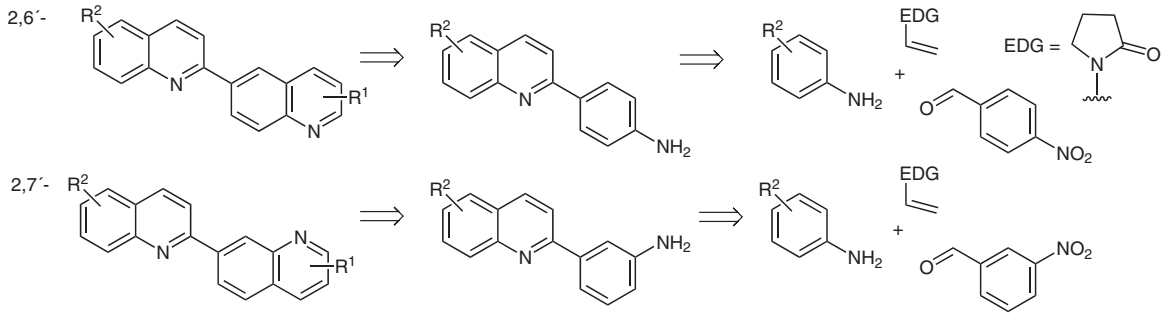
Key words: biquinoline derivatives, imino-Diels–Alder reactions, cycloadditions, intramolecular Friedel–Crafts reaction, cyclizations

Quinoline and tetrahydroquinoline structures are essential features of many natural products. These heterocycles play a key role in organic and medicinal chemistry. Their synthesis by various methodologies has been published extensively.[1–4] Compared to these systems, general synthetic methods for the preparation of diversely linked biquinolines are less developed.[5–8] Among the biquinolines, the 2,2′-biquinoline framework is the best known, because of its excellent ability as ligand in coordination chemistry.[9–13]

In addition, these compounds also represent interesting models for drug development, especially as anticancer agents. As part of our research programme on *N*-arylimines towards the synthesis of bioactive substituted tetrahydroquinolines and quinolines, we are investigating the synthesis of small drug-like molecules containing two different quinoline nuclei, whose synthesis could be accomplished by cycloaddition and/or cyclization reactions.

Therefore, the proposed routes for these systems were elaborated by retrosynthetic analysis for four different biquinoline structures. The synthesis of 2,6′- and 2,7′-biquinoline derivatives is based mainly on acid-catalyzed three-component imino-Diels–Alder reactions of simple anilines, benzaldehydes, and *N*-vinylpyrrolidin-2-one (Scheme 1). Construction of the 2,2′- and 2,8′-biquinoline derivatives is based on cationic intramolecular Friedel–Crafts cyclization of *N*-aryl-*N*-(quinolylbut-3-enyl)amines (‘homoallylamines’) (Scheme 2). Both synthetic approaches utilize simple anilines and aldehydes, whose reactions could lead to the formation of *N*-aryl aldimines, important participants in these synthetic transformations.

In this paper, we disclose a new design for the construction of diversely linked 2,6′- and 2,7′-biquinoline derivatives. Additionally, we wish to report a simple and efficient two-step synthesis of 2,2′- and 2,8′-biquinoline derivatives by 6-*exo-trig* reactions of the *N*-aryl-*N*-(quinolylbut-3-enyl)amines derived from the respective aldimines. The key (tetrahydro)quinoline compounds **4**–**13** (Scheme 3) in our synthetic plan for novel 2,6′- and 2,7′-biquinoline derivatives were prepared on the basis of



Scheme 1 Retrosynthetic analysis for 2,6′- and 2,7′-biquinolines by imino-Diels–Alder methodology

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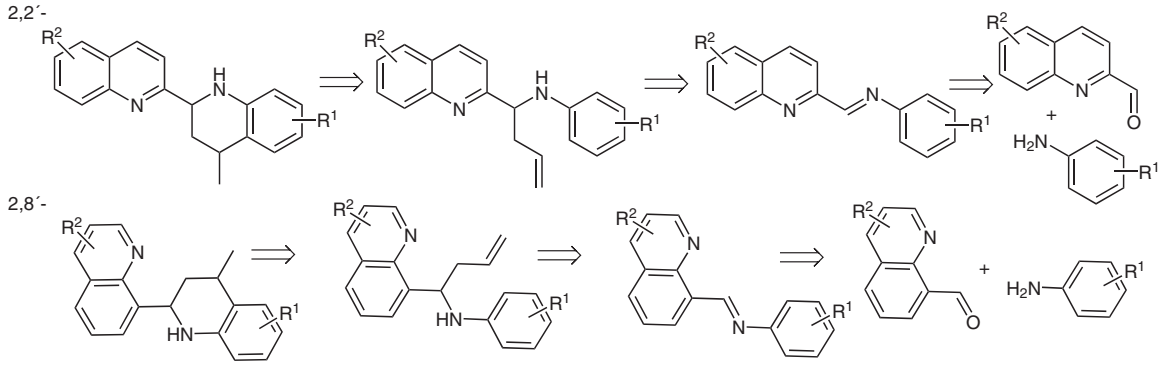


Scheme 2 Retrosynthetic analysis for 2,2′- and 2,8′-biquinolines by intramolecular Friedel–Crafts methodology

Table 1 (Tetrahydro)quinoline Compounds **4–13**

Compound	R^1	R^2	R^3	2-Aryl group	Yield (%)
4	H	H	H	*m*-$O_2NC_6H_4$	93
5	H	Me	H	*m*-$O_2NC_6H_4$	70
6	H	H	OMe	*m*-$O_2NC_6H_4$	81
7	H	Me	H	*p*-$O_2NC_6H_4$	95
8	Me	H	Me	*p*-$O_2NC_6H_4$	98
9	H	H	H	*m*-$H_2NC_6H_4$	95
10	H	Me	H	*m*-$H_2NC_6H_4$	92
11	H	H	OMe	*m*-$H_2NC_6H_4$	98
12	H	Me	H	*p*-$H_2NC_6H_4$	54
13	Me	H	Me	*p*-$H_2NC_6H_4$	94

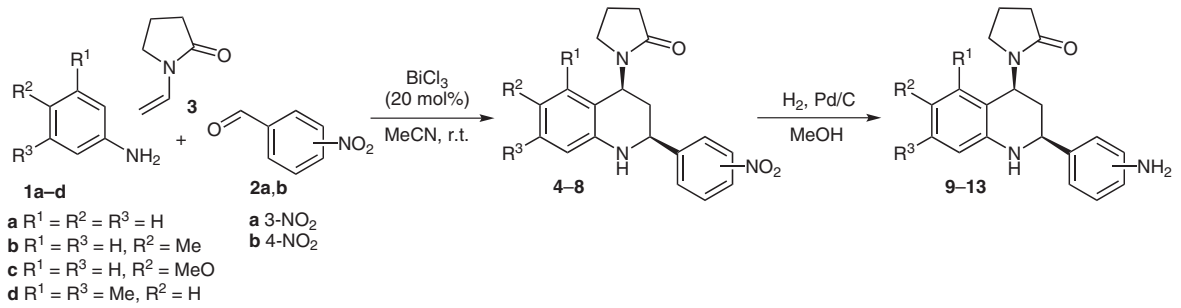
Table 2 New Biquinoline Derivatives **19–24**

Compound	R^1	R^2	R^3	2-Aryl group	Yield (%)
14	H	H	H	*m*-$H_2NC_6H_4$	70
15	H	Me	H	*m*-$H_2NC_6H_4$	85
16	H	OMe	H	*m*-$H_2NC_6H_4$	80
17	H	Me	H	*p*-$H_2NC_6H_4$	89
18	Me	H	Me	*p*-$H_2NC_6H_4$	73
19	H	H	H	–	58
20	H	Me	H	–	60
21	H	OMe	H	–	65
22	Me	H	Me	–	70
23	H	Me	H	–	33
24	Me	H	Me	–	40

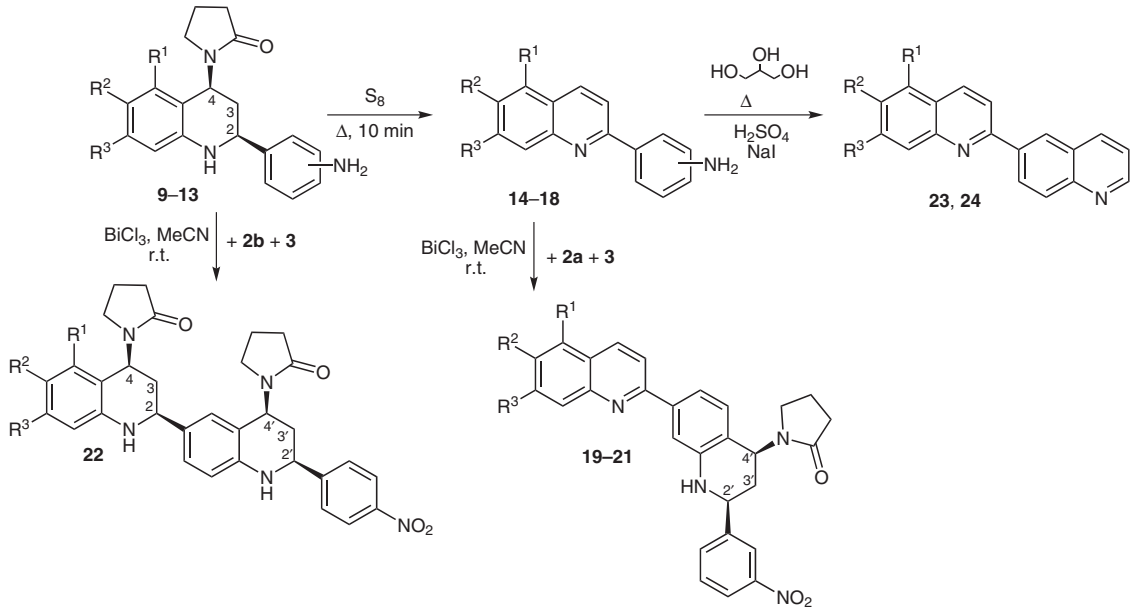
our experience in the construction of diverse heterocycles containing nitrogen, by means of a multicomponent Povarov reaction.[14–16]

First, the selected tetrahydroquinoline molecules **4–8** were easily synthesized by means of a bismuth(III) chloride catalyzed three-component imino-Diels–Alder cycloaddition reaction between substituted anilines **1a–d**, nitrobenzaldehydes **2a**,**b**, and *N*-vinylpyrrolidin-2-one (**3**; NVP) (Scheme 3).[17] These reactions proceeded smoothly in acetonitrile at room temperature to give the final products, substances easy to purify and manipulate. Hydrogenation (H_2/Pd/C, MeOH)[18] of these compounds gave the corresponding (aminophenyl)tetrahydroquinoline derivatives **9–13**, which were obtained as stable solids with well-defined *cis* stereochemistry (Scheme 3, Table 1). The *cis* configuration of the C2 and C4 substituents on the tetrahydroquinoline ring was determined by measurement of the corresponding H–H coupling constants in ^{1}H NMR spectra.[17]

With these suitable precursors **9–13** for the synthesis of the desired 2,6′- and 2,7′-biquinoline derivatives in our hands, we carried out an oxidation reaction with elemental sulfur (rapid fusion), which was accompanied by the loss of the pyrrolidinone fragment to afford 2-(*m*- or *p*-amino-



Scheme 3 Preparation of key (tetrahydro)quinoline compounds **4–13**



Scheme 4 Synthesis of new 2,6′- and 2,7′-biquinoline derivatives

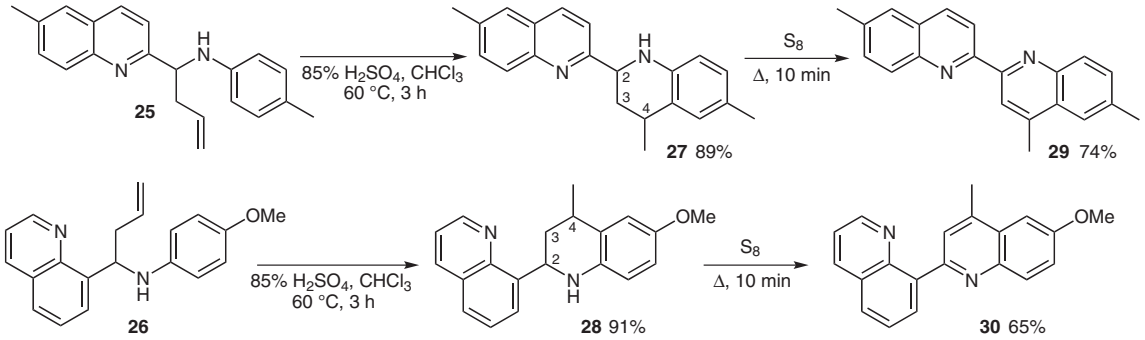
phenyl)quinolines **14**–**18** in excellent yields (Scheme 4, Table 2). The final steps of our synthesis consisted of the use of the same tactics and reagents employed in the initial step (reiterative process), to furnish the new 7-(2′-quinolyl)-1,2,3,4-tetrahydroquinolines **19**–**21** or 2,6′-bi(tetrahydroquinoline) **22**, obtained in moderate to good yields from nitrobenzaldehydes **2a** or **2b** and **3**.

On the other hand, when 2-(*p*-aminophenyl)quinolines **17** and **18** were employed as amino components in the Skraup reaction[18] of glycerol in the presence of sulfuric acid and sodium iodide, new 2,6′-biquinolines **23** and **24** were produced in moderate to good yields (Scheme 4, Table 2).

Finally, other biquinoline systems could be synthesized; for example, 2,2′- and 2,8′-biquinoline systems **29** and **30** were obtained by three synthetic steps from the corresponding *N*-[1-(6-methyl-2-quinolyl)but-3-enyl]-*N*-(*p*-tolyl)amine (**25**) and *N*-(*p*-methoxyphenyl)-*N*-[1-(8-quinolyl)but-3-enyl]amine (**26**), which were readily prepared from the corresponding quinolinecarboxaldehydes and primary anilines (Scheme 5).[19,20] Acid-mediated (85% H_2SO_4) intramolecular cyclization of homoallylamines **25** and **26** straightforwardly gave the corresponding 2-(2′-quinolyl)- and 2-(8′-quinolyl)-1,2,3,4-tetrahydroquinolines **27** and **28** in good yields. Rapid fusion of these tetrahydroquinolines with elemental sulfur (200 °C, 10 min) furnished the corresponding 2,2′-biquinoline **29** and 2,8′-biquinoline **30** as stable yellow substances (Scheme 5).

The structures of all the precursors as well as the final products were consistent with their IR and ^{1}H- and ^{13}C NMR spectra and supported by their MS data. ^{1}H and ^{13}C NMR analysis of the tetrahydroquinoline products indicated that the structure of the major diastereomers **4**–**8** and **9**–**13** was the *cis*-(2e,4e) form (as shown in Scheme 1). The large vicinal coupling constants $J_{2a,3a}$ and $J_{3a,4a}$ = 9.9–11.0 Hz for this form indicate an axial–axial (*trans*) relationship and the aryl groups on C2 and C4 are both pseudo-equatorial and located in the *cis* configuration. Isolated biquinoline products **19**–**21** display the same behavior, showing a *cis* configuration of the two substituents at the reduced ring. With regard to the spatial structure of bi(tetrahydroquinoline) ring **22**, it appears to also have a 'double' *cis* configuration.

From GC-MS analysis, the (quinolyl)tetrahydroquinoline **28** (Scheme 5) exists as a unique diastereomer [4e-Me/2e-



Scheme 5 Two-step procedure for the preparation of new 2,2′- and 2,8′-biquinoline derivatives

(8′-Qu)] (t_R = 44.92 min), whereas (quinolyl)tetrahydroquinoline **27** consists of a mixture of the two geometric isomers [4-Me/2-(2′-Qu)] in a ratio of 1:2 (t_R = 42.06, 44.01 min). According to NMR analysis of compound **28**, the methyl group and the quinoline ring are in *cis* configuration, both placed equatorially at C4 ($J_{4a,3a}$ = 12.1, $J_{4a,3e}$ = 6.0 Hz) and C2 ($J_{2a,3a}$ = 11.6, $J_{2a,3e}$ = 2.5 Hz), respectively. On the basis of the ^{1}H NMR data ($J_{4a,3a}$, $J_{2a,3a}$) and comparison with previous data for analogous tetrahydroquinolines,[21,22] we assumed that the major isomer (t_R = 44.01 min) of mixture **27** also has the *cis* configuration.

In conclusion, we have described new and efficient routes for diversely linked biquinoline derivatives, which represent interesting biological models in drug development; some of them are also potential ligands in coordination chemistry.

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. IR spectra of samples prepared as KBr pellets were obtained on a Lumex Infralum FT-02 or Nicolet Avatar 360-FTIR spectrometer. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were measured on a Bruker AM-400 spectrometer; $CDCl_3$ was used as the solvent. A Hewlett-Packard (HP) 5890 A series II gas chromatograph interfaced to an HP 5972 mass-selective detector with an HP MS ChemStation data system was used for MS at 70 eV {60 m capillary column, coated with HP-5 [5% phenylpoly(dimethylsiloxane)]; oven temperature 100 °C (3 min) to 200 °C (5 min) at 10 °C/min, then 280 °C (40 min) at 15 °C/min; ionization chamber and transfer line temperatures 230 and 285 °C, respectively}. The reaction progress was monitored by TLC (Merck Kieselgel 60, 230–240 mesh). Final purification of all products for elemental analyses was by recrystallization.

N-[2-(Nitrophenyl)-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-ones 4–8; General Procedure

A mixture of the arylamine **1** (16.5 mmol) and aldehyde **2** (19.8 mmol) in anhyd MeCN (15 mL) was stirred at r.t. for 30 min. $BiCl_3$ (20 mol%) was added. Over a period of 20 min, a soln NVP (**3**; 24.75 mmol) in MeCN (10 mL) was added dropwise. The resulting mixture was stirred for 10–14 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3 × 15 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo, and the resulting product was purified by column chromatography (silica gel, PE–EtOAc); this afforded the pure tetrahydroquinolines. The data of tetrahydroquinolines **4–6** have been published previously.[17]

N-[6-Methyl-2-(4-nitrophenyl)-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-one (7)

Yellow crystals; mp 222–223 °C.

IR (KBr): 3394, 2947, 2916, 1666, 1620 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.7 Hz, 2 H, 3(5)-H_{Ar}), 7.61 (d, J = 8.7 Hz, 2 H, 2(6)-H_{Ar}), 6.90 (dd, J = 8.0, 1.7 Hz, 1 H, 7-H_{THQ}), 6.68 (s, 1 H, 5-H_{THQ}), 6.57 (d, J = 8.1 Hz, 1 H, 8-H_{THQ}), 5.69 (dd, J = 11.1, 6.4 Hz, 1 H, 4-H_{THQ}), 4.65 (dd, J = 10.7, 3.1 Hz, 1 H, 2-H_{THQ}), 4.03 (br s, 1 H, 1-H_{THQ}), 3.21 (t, J = 6.9 Hz, 2 H, 5-H), 2.59–2.41 (m, 2 H, 3-H), 2.23 (s, 3 H, 6-CH_3), 2.13–1.99 (m, 4 H, 3-H_{THQ} and 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8, 150.6, 147.4, 142.9, 129.0, 128.1, 127.3 (2 C), 126.9, 123.9 (2 C), 118.8, 115.4, 56.0, 48.1, 42.2, 35.3, 31.3, 20.5, 18.1.

GC-MS: t_R = 44.57 min, m/z (%) = 351 (8) [M$^+$], 265 (100).

Anal. Calcd for $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.50. Found C, 68.93; H, 6.55; N, 11.35.

N-[5,7-Dimethyl-2-(4-nitrophenyl)-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-one (8)

Yellow crystals; mp 239–240 °C.

IR (KBr): 3271, 2972, 2916, 2854, 1666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.7 Hz, 2 H, 3(5)-H_{Ar}), 7.62 (d, J = 8.6 Hz, 2 H, 2(6)-H_{Ar}), 6.47 (s, 1 H, 6-H_{THQ}), 6.37 (s, 1 H, 8-H_{THQ}), 5.57 (t, J = 8.5 Hz, 1 H, 4-H_{THQ}), 4.48 (dd, J = 10.6, 2.5 Hz, 2 H, 2-H_{THQ}), 3.97 (br s, 1 H, 1-H_{THQ}), 3.08 (ddd, J = 9.7, 8.7, 5.4 Hz, 1 H, 5-H_e), 2.82 (ddd, J = 9.9, 8.4, 6.0 Hz, 1 H, 5-H_a), 2.43–2.27 (m, 3 H, 3-H and 3-H_{THQ}), 2.23 (s, 3 H, 5-CH_3), 2.10 (t, 1 H, J = 12.0, 3-H_{THQ}), 2.06 (s, 3 H, 7-CH_3), 1.94–1.72 (m, 2 H, 4-H).

^{13}C NMR ($CDCl_3$): δ = 174.5, 150.5, 147.5, 146.8, 138.3, 138.2, 127.2, 127.2, 123.9, 123.9, 122.9, 115.1, 114.3, 55.5, 46.5, 42.5, 36.3, 31.1, 20.91, 19.3, 17.9.

GC-MS: t_R = 49.65 min, m/z (%) = 365 (8) [M$^+$], 279 (100).

Anal. Calcd for $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.50. Found: C, 69.12; H, 6.20; N, 11.37.

N-[2-(Aminophenyl)-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-ones 9–13; General Procedure

A mixture of one of compounds **4–8** (1.5 mmol), wet 10% Pd/C (cat.), and MeOH (100 mL) was stirred under H_2 (1 atm) at r.t. for 14–16 h. The reaction mixture was filtered; the filtrate was concentrated in vacuo and extracted with EtOAc (3 × 15 mL). The organic layer was separated and dried (Na_2SO_4) and concentrated in vacuo, and the resulting product was purified by column chromatography (silica gel, PE–EtOAc); this afforded the corresponding pure product. The data of **9–11** have been published previously.[17]

N-[2-(4-Aminophenyl)-6-methyl-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-one (12)

Yellow crystals; mp 238–240 °C.

IR (KBr): 3456, 3425, 3317, 2947, 1666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 8.4 Hz, 1 H, 2-H_{Ar}), 8.18 (d, J = 8.3 Hz, 1 H, 6-H_{Ar}), 7.70 (dd, J = 11.5, 8.7 Hz, 2 H, 3(5)-H_{Ar}), 6.90 (bt, J = 5.5 Hz, 1 H, 7-H_{THQ}), 6.69 (s, 1 H, 5-H_{THQ}), 6.55 (t, J = 6.9 Hz, 1 H, 8-H_{THQ}), 5.71 (dd, J = 10.2, 6.9 Hz, 1 H, 4-H_{THQ}), 4.62 (ddd, J = 12.0, 10.6, 3.4 Hz, 1 H, 2-H_{THQ}), 3.96 (s, 1 H, 1-H_{THQ}), 3.20 (bd, J = 5.9 Hz, 2 H, 5-H), 2.59–2.43 (m, 2 H, 3-H), 2.23 (s, 3 H, 6-CH_3), 2.12–1.01 (m, 4 H, 3-H and 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8, 150.6, 143.0, 129.6, 129.1, 128.2, 128.1, 127.3, 127.1, 123.9, 119.0, 115.5, 56.2, 48.3, 42.3, 35.4, 31.3, 20.8, 20.5, 18.2.

GC-MS: t_R = 25.34 min, m/z (%) = 321 (1) [M$^+$], 234 (100).

Anal. Calcd for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 75.66; H, 7.39; N, 13.15.

N-[2-(4-Aminophenyl)-5,7-dimethyl-1,2,3,4-tetrahydro-4-quinolyl]pyrrolidin-2-one (13)

Yellow crystals; mp 185–186 °C.

IR (KBr): 3440, 2916, 1666, 1620, 1589 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, J = 8.2 Hz, 1 H, 2-H_{Ar}), 8.18 (d, J = 8.1 Hz, 1 H, 6-H_{Ar}), 7.55 (dd, J = 11.6, 8.9 Hz, 2 H, 3(5)-H_{Ar}), 6.45 (d, J = 5.9 Hz, 1 H, 6-H_{THQ}), 6.36 (d, J = 4.3 Hz, 1 H, 8-H_{THQ}), 5.58 (t, J = 8.5 Hz, 1 H, 4-H_{THQ}), 4.42 (t, J = 12.1 Hz, 1 H, 2-H_{THQ}), 3.97 (s, 1 H, 1-H_{THQ}), 3.11 (dd, J = 14.1, 8.5 Hz, 1 H, 5-H_e), 2.82 (dd, J = 15.3, 7.8 Hz, 1 H, 5-H_a), 2.41 - 2.31 (m, 3 H, 3-H and 3-H_{THQ}), 2.22 (s, 3 H, 5-CH_3), 2.11 (t, J = 12.0 Hz, 1 H, 3-H_{THQ}), 2.07 (s, 3 H, 7-CH_3), 1.85 (dd, J = 13.8, 6.0 Hz, 2 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 147.9, 145.9, 138.2, 137.7, 132.8, 127.4, 122.1, 115.2, 115.1, 114.3, 113.9, 55.5, 46.5, 42.5, 36.3, 31.1, 20.9, 19.3, 17.9.

GC-MS: t_R = 26.62 min, *m*/*z* (%) = 335 (1) [M$^+$], 248 (100).

Anal. Calcd for $C_{21}H_{25}N_3O$: C, 75.19; H, 7.51; N, 12.53. Found: C, 75.25; H, 7.68; N, 12.39.

2-(Aminophenyl)quinolines 14–18; General Procedure

A mixture of one of tetrahydroquinoline precursors **9**–**13** (0.5 mmol) and homogenated elemental sulfur (1.5 mmol) was heated at 260–280 °C for 10–15 min. The reaction mixture was purified by column chromatography (silica gel, PE–EtOAc) to afford the pure product, one of **14**–**18**.

2-(3-Aminophenyl)quinoline (14)

Yellow crystals; mp 111–112 °C.

IR (KBr): 3428, 3310, 3207, 2917, 2849 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 8.3, 3.0 Hz, 1 H, 8-H_{Qu}), 8.18 (d, *J* = 8.6 Hz, 1 H, 4-H_{Qu}), 7.81 (d, *J* = 8.6 Hz, 1 H, 3-H_{Qu}), 7.80 (d, *J* = 7.3 Hz, 1 H, 5-H_{Qu}), 7.72 (t, *J* = 8.1 Hz, 1 H, 7-H_{Qu}), 7.57 (br s, 1 H, 2-H_{Ar}), 7.51 (t, *J* = 7.8 Hz, 1 H, 6-H_{Qu}), 7.47 (d, *J* = 7.8 Hz, 1 H, 5-H_{Ar}), 7.29 (t, *J* = 7.8 Hz, 1 H, 4-H_{Ar}), 6.78 (dd, *J* = 7.8 Hz, 1 H, 1.5 Hz, 3-H_{Ar}), 3.57 (br s, 2 H, H_2N_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 147.9, 146.9, 140.5, 136.8, 129.8, 129.7, 129.5, 127.4, 127.2, 126.2, 119.2, 117.9, 116.3, 114.2.

MS (EI, 70 eV): *m*/*z* (%) = 220 (100) [M$^+$].

Anal. Calcd for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.50; H, 5.30; N, 12.65.

2-(3-Aminophenyl)-6-methylquinoline (15)

Yellow crystals; mp 100–101 °C.

IR (KBr): 3403, 3297, 3207, 3059, 2914 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.6 Hz, 1 H, 8-H_{Qu}), 7.97 (d, *J* = 8.6 Hz, 1 H, 3-H_{Qu}), 7.70 (d, *J* = 8.6 Hz, 1 H, 4-H_{Qu}), 7.55 (br s, 1 H, 5-H_{Qu}), 7.51 (dd, *J* = 8.6, 2.0 Hz, 1 H, 7-H_{Qu}), 7.48 (br s, 1 H, 2-H_{Ar}), 7.47 (ddd, *J* = 7.8, 2.2, 0.8 Hz, 1 H, 6-H_{Ar}), 7.30 (t, *J* = 7.8 Hz, 1 H, 5-H_{Ar}), 6.77 (ddd, 1 H, *J* = 7.8, 2.2, 0.8, 4-H_{Ar}), 3.82 (br s, 2 H, H_2N_{Ar}), 2.50 (s, 3 H, 6-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 146.9, 146.8, 140.9, 136.1, 135.9, 131.9, 129.7, 129.3, 127.3, 126.4, 119.2, 117.9, 116.1, 114.1, 21.6.

MS (EI, 70 eV): *m*/*z* (%) = 234 (100) [M$^+$].

Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.13; H, 6.19; N, 11.65.

2-(3-Aminophenyl)-6-methoxyquinoline (16)

Yellow crystals; mp 102–103 °C.

IR (KBr): 3376, 3305, 3183, 3065, 3013 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 9.1 Hz, 1 H, 4-H_{Qu}), 8.04 (d, *J* = 9.1 Hz, 1 H, 3-H_{Qu}), 7.78 (d, *J* = 8.3 Hz, 1 H, 8-H_{Qu}), 7.52 (br s, 1 H, 5-H_{Qu}), 7.44 (d, *J* = 8.3 Hz, 1 H, 7-H_{Qu}), 7.39 (dd, *J* = 8.0, 2.0 Hz, 1 H, 6-H_{Ar}), 7.28 (t, *J* = 7.8 Hz, 1 H, 5-H_{Ar}), 7.05 (br s, 1 H, 2-H_{Ar}), 6.75 (d, *J* = 7.8 Hz, 1 H, 4-H_{Ar}), 3.92 (s, 3 H, 6-CH_3O), 3.79 (br s, 2 H, H_2N_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 154.8, 146.6, 143.9, 140.5, 134.9, 130.8, 129.3, 127.8, 121.8, 119.0, 117.3, 115.5, 113.5, 104.7, 55.2.

MS (EI, 70 eV): *m*/*z* (%) = 250 (70) [M$^+$].

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.61; H, 5.79; N, 11.32.

2-(4-Aminophenyl)-6-methylquinoline (17)

Yellow crystals; mp 178–179 °C.

IR (KBr): 3386, 3301, 3193, 3055, 3023 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.7 Hz, 1 H, 3-H_{Qu}), 8.01 (m, 3 H, 2(6)-H_{Ar} and 8-H_{Qu}), 7.76 (d, *J* = 8.6 Hz, 1 H, 4-H_{Qu}), 7.53 (s, 1 H, 5-H_{Qu}), 7.52 (dd, *J* = 8.8, 1.3 Hz, 1 H, 7-H_{Qu}), 6.80 (dt, *J* = 8.6, 2.0 Hz, 2 H, 3(5)-H_{Ar}), 3.85 (br s, 2 H, H_2N_{Ar}), 2.53 (s, 3 H, 6-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 147.6, 146.9, 135.8, 135.3, 131.6, 130.1, 129.1, 128.6 (2 C), 126.8, 126.3, 118.3, 115.1 (2 C), 21.5.

GC-MS: t_R = 25.13 min, *m*/*z* (%) = 234 (100) [M$^+$].

Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 81.88; H, 6.15; N, 12.17.

2-(4-Aminophenyl)-5,7-dimethylquinoline (18)

Yellow crystals; mp 115–116 °C.

IR (KBr): 3433, 3317, 3201, 3032, 2962 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 8.9 Hz, 1 H, 3-H_{Qu}), 8.01 (d, *J* = 8.5 Hz, 2 H, 2(6)-H_{Ar}), 7.75 (s, 1 H, 8-H_{Qu}), 7.73 (d, *J* = 8.9 Hz, 1 H, 4-H_{Qu}), 7.13 (s, 1 H, 6-H_{Qu}), 6.79 (d, *J* = 8.5 Hz, 2 H, 3(5)-H_{Ar}), 3.85 (br s, 2 H, H_2N_{Ar}), 2.63 (s, 3 H, 7-CH_3), 2.50 (s, 3 H, 5-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 148.8, 147.6, 139.2, 133.8, 132.6, 130.0, 128.6 (2 C), 128.5, 126.7, 124.1, 117.0, 115.1 (2 C), 21.8, 18.4.

GC-MS: t_R = 26.94 min, *m*/*z* (%) = 248 (100) [M$^+$].

Anal. Calcd for $C_{17}H_{16}N_2$: C, 82.22; H, 6.49; N, 11.28. Found: C, 82.07; H, 6.67; N, 11.19.

***N*-[2′-(3-Nitrophenyl)-1′,2′,3′,4′-tetrahydro-2,7′-biquinolin-4′-yl]pyrrolidin-2-ones 19–21; General Procedure**

A mixture of one of anilines **14**–**18** (0.5 mmol) and aldehyde **2a** (0.55 mmol) in anhyd MeCN (15 mL) was stirred at r.t. for 30 min. $BiCl_3$ (20 mol%) was added. Over a period of 20 min, a soln NVP (**3**; 0.56 mmol) in MeCN (10 mL) was added dropwise. The resulting mixture was stirred for 10–14 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3 × 15 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo, and the resulting product was purified by column chromatography (silica gel, PE–EtOAc); this afforded the pure product.

***N*-[2′-(3-Nitrophenyl)-1′,2′,3′,4′-tetrahydro-2,7′-biquinolin-4′-yl]pyrrolidin-2-one (19)**

Yellow crystals; mp 134–136 °C.

IR (KBr): 3427, 3261, 2917, 1660, 1513 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (br s, 1 H, 2-H_{Ar}), 8.16 (d, *J* = 8.0 Hz, 1 H, 6′-H_{THQ}), 8.14 (d, *J* = 8.0 Hz, 1 H, 8-H_{Qu}), 8.12 (dd, *J* = 8.3, 2.0 Hz, 1 H, 4-H_{Ar}), 7.79 (d, *J* = 8.0 Hz, 1 H, 4-H_{Qu}), 7.71 (d, *J* = 8.0 Hz, 1 H, 3-H_{Qu}), 7.70 (t, *J* = 8.0 Hz, 1 H, 7-H_{Qu}), 7.70 (t, *J* = 8.0 Hz, 1 H, 5-H_{Ar}), 7.50 (br s, 1 H, 8′-H_{THQ}), 7.49 (d, *J* = 8.3 Hz, 1 H, 6-H_{Ar}), 7.22 (t, *J* = 8.0 Hz, 1 H, 6-H_{Qu}), 6.90 (d, *J* = 8.0 Hz, 5-H_{Qu}), 6.75 (d, *J* = 8.0 Hz, 1 H, 5′-H_{THQ}), 6.0 (dd, *J* = 12.0, 8.0 Hz, 1 H, 2′-H_{THQ}), 4.66 (dd, *J* = 12.0, 4.0 Hz, 1 H, 4′-H_{THQ}), 4.29 (br s, 1 H, 1′-H_{THQ}), 2.97–2.90 (m, 2 H, 5-H), 2.17–2.15 (m, 2 H, 3-H), 1.98–1.61 (m, 2 H, 3′-H_{THQ}), 1.15–1.12 (m, 2 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 159.3, 148.3, 147.7, 146.7, 144.9, 141.5, 135.8, 132.8, 129.7, 129.6, 129.2, 128.7, 127.5, 126.8, 126.3, 122.8, 121.5, 121.3, 121.2, 116.6, 116.4, 55.0, 47.0, 42.1, 35.3, 30.0, 16.7.

MS (EI, 70 eV): *m*/*z* (%) = 464 (70) [M$^+$].

Anal. Calcd for $C_{28}H_{24}N_4O_3$: C, 72.40; H, 5.21; N, 12.06. Found: C, 72.30; H, 5.15; N, 12.10.

_N_-[6-Methyl-2′-(3-nitrophenyl)-1′,2′,3′,4′-tetrahydro-2,7′-biquinolin-4′-yl]pyrrolidin-2-one (20)
Yellow crystals; mp 138–140 °C.

IR (KBr): 3405, 3325, 3208, 1667, 1527 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 (br s, 1 H, 2-H_{Ar}), 8.12 (dd, *J* = 8.0, 1.5 Hz, 1 H, 4-H_{Ar}), 8.07 (d, *J* = 8.6 Hz, 1 H, 4-H_{Qu}), 7.99 (d, *J* = 8.3, Hz, 1 H, 7′-H_{THQ}), 7.75 (d, *J* = 8.6 Hz, 1 H, 3-H_{Qu}), 7.67 (d, *J* = 7.6 Hz, 1 H, 8-H_{Qu}), 7.54 (br s, 1 H, 5-H_{Qu}), 7.52 (dd, 1 H, *J* = 7.6, 1.0, 7-H_{Qu}), 7.47 (t, *J* = 8.0 Hz, 1 H, 4-H_{Ar}), 7.42 (dd, *J* = 8.0, 1.5 Hz, 1 H, 5-H_{Ar}), 7.02 (d, *J* = 8.3 Hz, 1 H, 8′-H_{THQ}), 5.75 (dd, *J* = 11.0, 4.0 Hz, 1 H, 2′-H_{THQ}), 4.67 (dd, *J* = 11.0, 3.0 Hz, 1 H, 4′-H_{THQ}), 4.46 (br s, 1 H, 1′-H_{THQ}), 3.26 (t, 2 H, *J* = 7.0, 5-H), 2.57–2.46 (m, 2 H, 3′-H_{THQ}), 2.13–2.10 (m, 2 H, 3-H), 2.07–2.02 (m, 2 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 156.0, 148.6, 146.6, 145.9, 145.1, 140.0, 136.2, 136.1, 132.8, 132.0, 129.6, 129.2, 127.4, 127.3, 126.3, 122.9, 121.4, 120.1, 118.8, 117.9, 114.4, 55.8, 48.2, 42.3, 35.3, 31.3, 21.5, 18.3.

MS (EI, 70 eV): *m*/*z* (%) = 478 (80) [M^+].

Anal. Calcd for $C_{29}H_{26}N_4O_3$: C, 72.79; H, 5.48; N, 11.71. Found: C, 72.50; H, 5.25; N, 11.10.

_N_-[6-Methoxy-2′-(3-nitrophenyl)-1′,2′,3′,4′-tetrahydro-2,7′-biquinolin-4′-yl]pyrrolidin-2-one (21)
Yellow crystals; mp 156–158 °C.

IR (KBr): 3407, 3322, 3205, 1669, 1522 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.27 (br s, 1 H, 2-H_{Ar}), 8.14 (dd, *J* = 8.0, 1.5 Hz, 1 H, 4-H_{Ar}), 8.08 (d, *J* = 8.0 Hz, 1 H, 7′-H_{THQ}), 8.07 (d, *J* = 8.0, Hz, 1 H, 4-H_{Qu}), 7.94 (d, *J* = 8.0 Hz, 1 H, 3-H_{Qu}), 7.73 (d, *J* = 8.0 Hz, 1 H, 8-H_{Qu}), 7.51 (t, *J* = 8.0 Hz, 1 H, 5-H_{Ar}), 7.49 (d, *J* = 8.0 Hz, 1 H, 7-H_{Qu}), 7.40 (d, *J* = 8.0 Hz, 1 H, 6-H_{Ar}), 7.36 (br s, 1 H, 5-H_{Qu}), 7.33 (br s, 1 H, 5′-H_{THQ}), 7.26 (d, *J* = 8.0 Hz, 8′-H_{THQ}), 5.37 (dd, *J* = 12.0, 4.0 Hz, 1 H, 2′-H_{THQ}), 4.53 (dd, *J* = 12.0, 4.0 Hz, 1 H, 4′-H_{THQ}), 4.39 (br s, 1 H, 1′-H_{THQ}), 3.42–3.23 (m, 2 H, 5-H), 2.40–2.35 (m, 2 H, 3′-H_{THQ}), 2.17–2.03 (m, 2 H, 3-H), 2.00–1.82 (m, 2 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 157.7, 156.9, 148.7, 146.7, 145.2, 143.9, 135.5, 134.7, 134.6, 133.0, 129.5, 127.8, 127.4, 123.0, 122.6, 122.4, 121.7, 120.9, 119.1, 117.8, 105.1, 55.6, 55.2, 48.2, 42.4, 35.5, 31.4, 18.3.

MS (EI, 70 eV): *m*/*z* (%) = 494 (80) [M^+].

Anal. Calcd for $C_{29}H_{26}N_4O_4$: C, 70.43; H, 5.30; N, 11.33. Found: C, 70.15; H, 5.25; N, 11.10.

5,7-Dimethyl-2′-(4-nitrophenyl)-4,4′-bis(2-oxopyrrolidin-1-yl)-1,1′,2,2′,3,3′,4,4′-octahydro-2,6′-biquinoline (22)
A mixture of aniline **13** (0.97 g, 2.9 mmol) and aldehyde **2b** (0.54 g, 3.6 mmol) in anhyd MeCN (15 mL) was stirred at r.t. for 30 min. $BiCl_3$ (0.18 g, 20 mol%) was added. Over a period of 20 min, a soln of NVP (**3**; 0.50 g, 4.5 mmol) in MeCN (10 mL) was added dropwise. The resulting mixture was stirred for 10–14 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with H_2O (30 mL) and extracted with EtOAc (3 × 15 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo, and the resulting product was purified by column chromatography (silica gel, PE–EtOAc, 4:1); this gave pure biquinoline **22**.

Yield: 1.18 g (70%); white powder; mp 150–152 °C.

IR (KBr): 3264, 2967, 1660, 1513, 1351 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.0 Hz, 2 H, 3(5)-H_{Ar}), 7.60 (d, *J* = 8.0 Hz, 2 H, 2(6)-H_{Ar}), 7.12 (dd, *J* = 8.0, 4.0 Hz, 1 H, 7′-H_{THQ}), 6.81 (br s, 1 H, 5-H_{THQ}); 6.65 (d, *J* = 8.0 Hz, 1 H, 8′-H_{THQ}), 6.39 (br s, 1 H, 7-H_{THQ}), 6.27 (d, *J* = 4.0 Hz, 1 H, 5′-H_{THQ}), 5.67 (dd, *J* = 12.0, 8.0 Hz, 1 H, 4-H_{THQ}), 5.53 (dd, *J* = 12.0, 8.0 Hz, 1 H, 4′-H_{THQ}), 4.68 (dd, *J* = 12.0, 4.0 Hz, 1 H, 2-H_{THQ}), 4.31 (br s, 1 H, 1′-H_{THQ}), 4.17 (dd, *J* = 12.0, 4.0 Hz, 1 H, 2′-H_{THQ}), 3.80 (br s, 1 H, 1-H_{THQ}), 3.22–3.00 (m, 4 H, 5-H), 2.90–2.50 (m, 4 H, 3(3′)-H_{THQ}), 2.19 (s, 3 H, 5-CH_3), 2.15–2.05 (m, 4 H, 3-H), 2.02 (s, 3 H, 7-CH_3), 1.98–1.85 (m, 4 H, 4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 174.4, 150.3, 147.9, 147.5, 138.2, 137.7, 135.1, 133.2, 127.2 (2 C), 126.3, 124.9, 123.9 (2 C), 122.3, 118.7 (2 C), 115.6, 114.2, 55.8, 55.3, 48.2, 48.1, 42.3 (2 C), 36.7, 35.1, 31.2 (2 C), 20.9, 19.4, 18.2 (2 C).

MS (EI, 70 eV): *m*/*z* (%) = 579 (90) [M^+].

Anal. Calcd for $C_{34}H_{37}N_5O_4$: C, 70.45; H, 6.43; N, 12.08. Found: C, 70.15; H, 6.10; N, 12.05.

2,6′-Biquinolines 23 and 24; General Procedure
A mixture of the appropriate 2-(aminophenyl)quinoline (0.4 mmol), concd H_2SO_4 (5 mL), and NaI (0.1 mmol) was stirred at 120 °C for 10 min. Then glycerol (0.05 g, 0.5 mmol) was added and the mixture was stirred at 150 °C for 3 h. After completion of the reaction as indicated by TLC, the reaction mixture was treated with 30% aq NaOH (10 mL) and extracted with EtOAc (3 × 15 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo, and the resulting product was purified by column chromatography (silica gel, PE–EtOAc, 4:1).

6-Methyl-2,6′-biquinoline (23)
Yellow crystals; mp 152–153 °C.

IR (KBr): 3039, 2916, 1589, 1481, 1365, 1311 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.95 (d, *J* = 4.2 Hz, 1 H, 2′-H), 8.58 (s, 1 H, 5′-H), 8.56(m, 1 H, 7′-H), 8.28 (d, *J* = 8.2 Hz, 1 H, 4′-H), 8.24 (d, *J* = 8.1 Hz, 1 H, 8′-H), 8.17 (d, *J* = 8.6 Hz, 1 H, 3-H), 8.10 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.97 (d, *J* = 8.6 Hz, 1 H, 4-H), 7.60 (s, 1 H, 5-H), 7.60 (m, 1 H, 7-H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1 H, 3′-H), 2.56 (s, 3 H, 6-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.4, 150.9, 148.7, 146.9, 137.8, 136.8, 136.5 (2 C), 136.3, 132.2 130.0, 129.4, 128.7, 126.6, 126.4, 121.5, 118.9, 21.6.

GC-MS: t_R = 27.51 min, *m*/*z* (%) = 270 (100) [M^+].

Anal. Calcd for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22; N, 10.36. Found: C, 84.65; H, 5.01; N, 10.28.

5,7-Dimethyl-2,6′-biquinoline (24)
Yellow crystals; mp 77–79 °C.

IR (KBr): 2954, 2924, 2854, 1666 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.85 (d, *J* = 4.3 Hz, 1 H, 2′-H), 8.70 (m, 1 H, 7′-H), 8.44 (s, 1 H, 5′-H), 8.37 (m, 1 H, 4′-H), 8.23 (d, *J* = 8.1 Hz, 1 H, 4-H), 8.09 (d, *J* = 8.6 Hz, 1 H, 8′-H), 7.60 (s, 1 H, 6-H), 7.57 (m, 1 H, 3′-H), 7.50 (s, 1 H, 8-H), 7.30 (m, 1 H, 3-H), 2.55 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.0, 149.8, 147.2, 146.8, 142.6, 139.8, 138.9, 136.4–133.0 (3 C), 129.5–127.0 (4 C), 123.3, 121.6, 117.8, 21.5, 19.7.

GC-MS: t_R = 29.70 min, *m*/*z* (%) = 284 (100) [M^+].

Anal. Calcd for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85. Found: C, 84.23; H, 5.88; N, 9. 91.

Tetrahydrobiquinolines 27 and 28; General Procedure

85% H_2SO_4 (2 mL) was added dropwise at 0 °C to the appropriate homoallylamine **25** or **26** (3.7 mmol) in $CHCl_3$ (3–5 mL), and the resulting mixture was heated at 60 °C for 3 h. Upon completion of the reaction (monitored by TLC), the mixture was cooled to r.t., concd NH_4OH soln was added to adjust the pH to 10, and the resulting mixture was extracted with Et_2O (3 × 50 mL). After removal of the solvent from the combined extracts, the oily residue was purified by column chromatography (silica gel, heptane–EtOAc, 20:1); this gave the corresponding tetrahydrobiquinoline **27** or **28**.

4,6,6′-Trimethyl-1,2,3,4-tetrahydro-2,2′-biquinoline (27)

Yield: 89%; yellow crystals; mp 201–202 °C.

IR (KBr): 3417, 1595 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, 1 H, *J* = 8.1 Hz, 3-H_{Qu}), 7.99 (dd, *J* = 8.6 Hz, 1 H, 8-H_{Qu}), 7.70–7.40 (m, 2 H, 4(7)-H_{Qu}), 7.58 (s, 1 H, 5-H_{Qu}), 7.01 (d, *J* = 1.9 Hz, 1 H, 5-H), 6.86 (dd, *J* = 7.3, 1.9 Hz, 1 H, 7-H), 6.59 (d, *J* = 7.9 Hz, 1 H, 8-H), 4.75 (dd, *J* = 11.6, = 3.1 Hz, 1 H, 2-H), 3.25 (sept, *J* = 11.2, 6.8, 5.3 Hz, 1 H, 4-H), 2.54 (s, 3 H, CH_{3Qu}), 2.09–2.00 (m, 1 H, 3-H_{eq}), 2.26 (s, 3 H, 6-CH_3), 1.78 (q, 1 H, *J* = 11.6, 11.6 Hz; 3-H_{ax}), 1.37 (d, 3 H, *J* = 6.8 Hz; 4-CH_3).

GC-MS: t_R = 42.06 and 44.01 min (ratio 1:2); t_R (minor isomer) = 42.06 min, *m*/*z* (%) = 302 (95) [M^+], 287 (99), 271 (5), 260 (5), 246 (1), 207 (4), 196 (2), 181 (2), 170 (14), 157 (78), 144 (100), 130 (24), 115 (28), 103 (4), 91 (12), 77 (8), 65 (7), 55 (4), 41 (7); t_R (major isomer) = 44.01 min, *m*/*z* (%) = 302 (99) [M^+], 287 (20), 273 (6), 259 (5), 245 (1), 207 (2), 195 (0.5), 182 (1), 170 (7), 160 (100), 144 (95), 130 (22), 115 (23), 102 (3), 91 (10), 77 (6), 65 (4), 55 (3), 41 (5).

Anal. Calcd for $C_{21}H_{22}N_2$: C, 83.44; H, 7.28; N, 9.27. Found: C, 83.25; H, 7.63; N, 9.15.

6-Methoxy-4-methyl-1,2,3,4-tetrahydro-2,8′-biquinoline (28)

Yield: 91%; yellow oil.

IR (neat): 3353, 1599 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.5 Hz, 1 H, 2-H_{Qu}), 7.84 (dd, *J* = 7.1 Hz, 1 H, 5-H_{Qu}), 7.67 (d, *J* = 8.1 Hz, 1 H, 7-H_{Qu}), 7.45 (dd, *J* = 8.4, 7.1 Hz, 2 H, 4(6)-H_{Qu}), 6.89 (dd, *J* = 8.5, 8.4 Hz, 1 H, 3-H_{Qu}), 6.85 (d, *J* = 2.6 Hz, 1 H, 5-H), 6.66 (dd, *J* = 8.6, 2.6 Hz, 1 H, 7-H), 6.57 (d, *J* = 8.6 Hz, 1 H, 8-H), 5.67 (dd, 1 H, *J* = 11.3, 2.0 Hz; 2-H), 3.79 (s, 3 H, OCH_3), 2.65 (sept, *J* = 12.0, 6.8, 5.5, Hz, 1 H, 4-H), 2.42 (ddd, *J* = 11.9, 5.5, 2.0 Hz, 1 H, 3-H_{eq}), 1.88 (q, *J* = 12.0, 11.9 Hz, 1 H, 3-H_{ax}), 1.40 (d, *J* = 6.8 Hz, 3 H, 4-CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 155.1, 152.3, 145.9, 141.5, 139.9, 136.6, 132.4, 128.4, 127.1, 126.6, 126.1, 118.9, 115.9, 113.2, 112.4, 55.9, 50.6, 39.1, 31.6, 20.7.

GC-MS: t_R = 44.92 min, *m*/*z* (%) = 304 (100) [M^+], 143 (86).

Anal. Calcd for $C_{20}H_{20}N_2O$: C, 78.95; H, 6.58; N, 9.21. Found: C, 78.85; H, 6.83; N, 9.11.

Biquinolines 29 and 30; General Procedure

A mixture of the appropriate tetrahydroquinoline **27** or **28** (0.5 mmol) and homogenated elemental sulfur (0.041 g, 1.3 mmol) was heated at 200 °C for 5–10 min until the evolution of gas (H_2S) ceased. The solid residue was purified by column chromatography (alumina, heptane–EtOAc, 50:1).

4,6,6′-Trimethyl-2,2′-biquinoline (29)

Yield: 74%; yellow crystals; mp 203 °C.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.98–7.27 (m, 9 H, H_{Qu}), 2.79 (s, 3 H, 4-CH_3), 2.58 (s, 3 H, 6′-CH_3), 2.55 (s, 3 H, 6-CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 157.8–119.4 (C-Qu), 21.9 (6′-CH_3), 21.7 (6-CH_3), 19.0 (4-CH_3).

GC-MS: t_R = 49.51 min, *m*/*z* (%) = 298 (100) [M^+].

Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.56; H, 6.04; N, 9.40. Found: C, 84.85; H, 6.33; N, 9.05.

6-Methoxy-4-methyl-2,8′-biquinoline (30)

Yield: 65%; yellow crystals; mp 208 °C.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.95–7.05 (m, 9 H, H_{Qu}), 3.80 (s, 3 H, OCH_3), 2.84 (s, 3 H, 4-CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.9–119.5 (C-Qu), 55.2 (6-CH_3O), 19.5 (4-CH_3).

GC-MS: t_R = 47.15 min, *m*/*z* (%) = 300 (100) [M^+].

Anal. Calcd for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33. Found: C, 79.81; H, 5.54; N, 9.23.

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