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# 6-*endo*-dig Cycloisomerization of *N*-Propargyl Aminoquinoxalines: A New Route to 1,4,8-Triazaphenanthrenes

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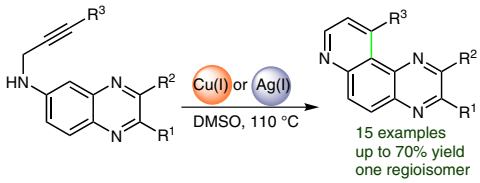
This paper is dedicated in the memory of Prof Jean F. Normant, a great mentor and a wonderful person.

‡ S.V. and G.L.D. contributed equally to this work.

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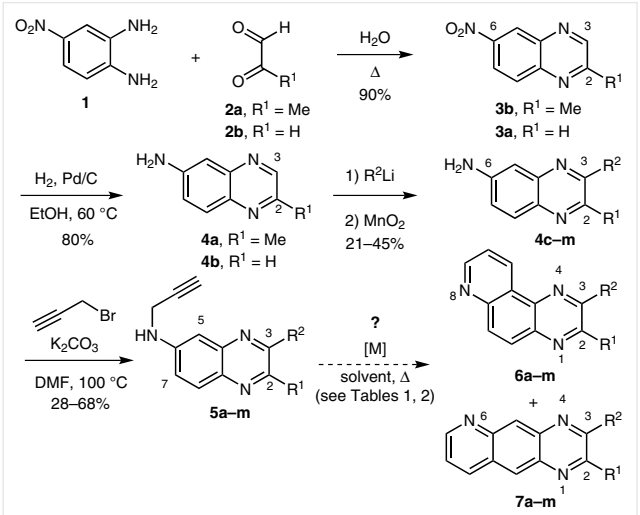
**Abstract** We report the preparation of novel 1,4,8-triazaphenanthrenes and show that the target compounds are efficiently obtained from the corresponding 6-aminoquinoxalines after N-propargylation followed by copper-catalyzed 6-*endo*-dig cycloisomerization and aromatization. The cyclization was found to be completely regioselective.

**Key words** copper, silver, regioselectivity, *N*-heterocycles, Lewis acids

We are currently involved in transition-metal-catalyzed synthesis of natural products[1] and bioactive compounds.[2a–i] Recently, we prepared a library of 2,3-disubstituted 6-aminoquinoxalines that showed interesting neuroprotective activities on dopaminergic neurons in primary cultures.[2i,3] We then prepared the *N*-propargyl derivatives of the latter and found that they also show interesting properties in several in vitro models of Parkinson's disease.[3] The 6-*endo*-dig cycloisomerization[4] of the *N*-propargyl-6-aminoquinoxalines, which has not been previously reported, could lead to tricyclic compounds, namely 1,4,6-triazaanthracenes[5] and/or 1,4,8-triazaphenanthrenes[6] (also named pyrido[2,3-*g*]quinoxaline and/or pyrido[3,2-*f*]quinoxaline), depending on the regioselectivity of the cyclization. *N*-Propargyl-6-aminoquinoxalines could be obtained in a straightforward manner from nitrophenylenediamine **1** after condensation with glyoxal **2b** or pyruvaldehyde **2a** to produce quinoxaline **3a** or **3b**, which, after hydrogenolysis, led to aminoquinoxaline **4a** and **4b**.[2i] Disubstituted quinoxalines were prepared by further addition of an aryllithium reagent on the more reactive 3-position of aminoquinoxaline **4a** and **4b**.[2f,i,3] Propargylation of the amino group furnished the desired *N*-propargyl-6-aminoquinoxaline **5a**–**m**.[3] The 6-*endo*-dig cycloisomerization of quinoxalines **5a**–**m** led, after further spontaneous aromatization, to 1,4,6-triazaanthracene **6a**–**m** or 1,4,8-triazaphenanthrene **7a**–**m** (Scheme 1).

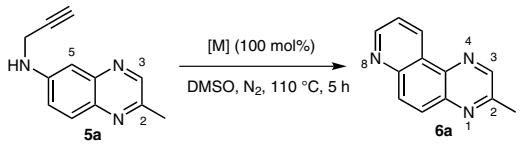



**Scheme 1** Access to *N*-propargyl-6-aminoquinoxalines **5a**–**m**

The 6-*endo*-dig cycloisomerization is a well-known process that can be performed thermally through a Claisen-type rearrangement[4a] under high temperature, under harsh conditions ($BF_3$·OEt),[4o] by using metal-catalysis with noble metals (platinum,[4c] gold,[4b,f,g,j,m,q,s] palladium[4p]), toxic metals (mercury[4k]), substrate-dependent metals (iron[4l,r] and indium[4t]), or by using electrophilic reagents (such as halonium and selenium but these lead to halogeno or seleno-cyclized products).[4e,k] Thus, benign and affordable metal catalysts such as silver[4h,s] and copper,[4e,f,i] were studied to perform this reaction. When **5a** was heated at reflux in toluene for 5 hours in the presence of CuCl (1 equiv), under the report-

ed conditions for cyclization of *N*-propargylanilines,[4e] 1,4,8-triazaphenanthrene **7a** was isolated as the sole product in 30% yield (Table 1, entry 1) along with some unreacted starting material **5a**. We found, however, that the reaction works better in dimethyl sulfoxide (DMSO) (60% yield, entry 2). It is important to stress that a stoichiometric amount of catalyst is needed to reach almost full conversion, which is probably due to deactivation of the catalyst by chelation with the product, as observed in a previous report.[4e] The influence of the nature of catalyst (used in a stoichiometric amount) was then studied, using DMSO as solvent. Copper(II) catalysts were quite ineffective (entries 8 and 9), whereas the hardest counter-anions for copper(I) (in the meaning of the HSAB theory) worked best for this reaction ($CuPF_6(MeCN)_4$ vs. $Cu_2O$; entries 3 and 4). In contrast, the softer the counter-anion is, the worse the cycloisomerization is (CuBr, CuI, CuCN; entries 5, 6, and 7, respectively).

**Table 1** Effect of the Transition-Metal Catalyst on the 6-*endo*-dig Cycloisomerization of Aminoquinoxaline[5a]




| Entry | Catalyst | Yield (%)[c] | Entry | Catalyst | Yield (%)[c] |
|---|---|---|---|---|---|
| 1 | CuCl[a] | 30 | 11 | $Ag_2CO_3$ | 25 |
| 2 | CuCl | 60 | 12 | $Ag_2O$ | 30 |
| 3 | $CuPF_6(MeCN)_4$ | 71 | 13 | AgF | 57 |
| 4 | $Cu_2O$ | 70 | 14 | $AgNO_3$ | 67 |
| 5 | CuBr | 41 | 15 | AgOCN | 58 |
| 6 | CuI | 22 | 16 | $AgSbF_6$ | 58 |
| 7 | CuCN | 13 | 17 | $CF_3CO_2Ag$ | 60 |
| 8 | $CuCl_2$ | 20 | 18 | AcOAg | 30 |
| 9 | $Cu(AcO)_2$ | 0 | 19 | $NaAuCl_4$[d] | 39 |
| 10 | $Cu_2O$[b] | 44 | 20 | none | 0 |

[a] Reaction performed in toluene.
[b] Reaction performed under air atmosphere.
[c] Isolated yield.
[d] 10 mol% $NaAuCl_4$ was used.

We also studied the effect of silver salts, and found that the reaction was as effective as with copper(I) salts; however, several observations can be made. The reactivity of silver salts follows the general observation noted for copper(I) salts (AgF; Table 1, entry 13, 57%), but the basicity of the counter-anion was also important for the reactivity. The best example is given by silver trifluoroacetate (60% yield, entry 17), which gave a higher yield than with silver acetate (30% yield, entry 18). $Ag_2O$ was also not efficient, in contrast to $Cu_2O$ (30% yield, entry 12). In general, less basic counter-anions gave the best results. In particular, the use of silver nitrate led to the best yield for this transformation (67%, entry 14). This observation was already reported for the synthesis of acridines though 6-*endo*-dig cycloisomerization.[4h] Here again, a stoichiometric amount of silver salt is necessary to reach full conversion. Gold was briefly studied, but the use of a stoichiometric amount of $NaAuCl_4$ is not feasible because of the high cost of the metal, thus when **5a** was treated with 0.1 equiv of $NaAuCl_4$ the desired compound **6a** was obtained in a reasonable yield (39% yield, entry 19). Notably, in the absence of any catalyst, heating **5a** at 110 °C, or above, in DMSO for 4 hours did not give the desired product, and starting material was recovered unchanged (entry 20). The reaction is also less efficient in the presence of air, probably due to some oxidation of Cu(I) into less active Cu(II) (entry 10).

To explain the complete regioselectivity of **5a** cyclization yielding only 1,4,8-triazaphenanthrene **6a**, we calculated the frontier molecular orbitals (FMO) of the starting materials (see the Supporting Information). DFT calculations conducted on the unsubstituted quinoxaline **5b** showed a much higher electronic density in the HOMO at the 5-position than at the 7-position, thus directing the cyclization to afford the corresponding 1,4,8-triazaphenanthrene **6b** (Figure 1). Blocking the 5-position of compound **5b** by the presence of a chlorine atom did not allow us to obtain the corresponding 1,4,6-triazaanthracene (results not shown). The low electronic density of HOMO at the 7-position of the latter could, again, explain the lack of reactivity (no significant difference was observed for the FMO of both compounds).

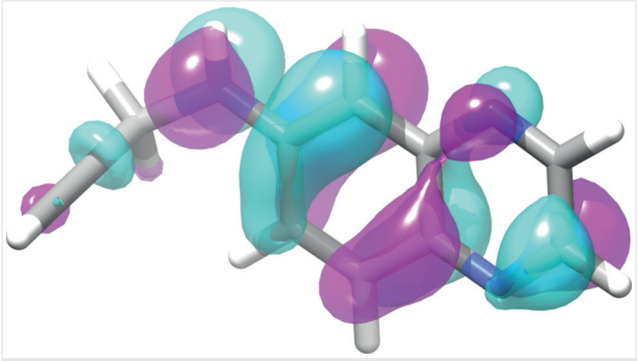
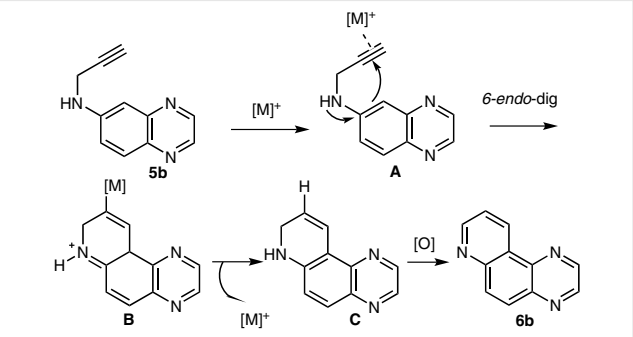


**Figure 1** Electronic isodensity surface at 50% probability level for the highest occupied molecular orbital (HOMO) of *N*-propargyl-6-aminoquinoxaline **5b**, calculated at the B3LYP/6-31G* level (the colour of the surfaces indicates the sign of the wavefunction)

The cycloisomerization was applied to *N*-propargyl-6-aminoquinoxaline derivatives **5b**–**m** (see Table 2). Less expensive copper-mediated catalysis rather than silver was applied to most examples. $Cu_2O$ gave generally the best yield, as shown in Table 2; however, CuCl was used for some examples and nevertheless gave decent yields. The transformation takes place with a compound having no substituent in positions 2 and 3 (entry 1), having one substituent in po-

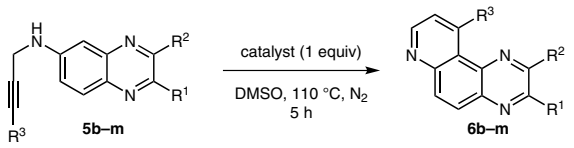
sition 2 (entry 2) or two substituents at positions 2 and 3 (entries 3–11). Not only terminal alkynes react, disubstituted alkynes are also suitable; indeed, compound **5m** cycloisomerized in the presence of $AgNO_3$ (entry 12) to give 1,4,8-triazaphenanthrene **6m** in moderate 43% yield, although copper was ineffective in this case.

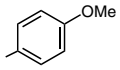
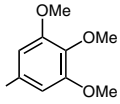
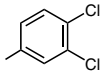
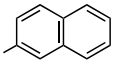
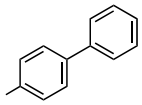
The mechanism of the reaction is thought to proceed through a Claisen-type reaction, in which the catalyst activates the triple bond of **5b** by coordination, as presented in intermediate **A** (Scheme 2). The ability of the metal to be coordinated is directly linked to the ionic character of the utilized salt, as shown in our study. Once activated, the double bond attacks the electropositive triple bond from




**Scheme 2** Putative mechanism for the cyclization of quinoxaline **5b**

**Table 2** 6-*endo*-dig Cycloisomerization of Quinoxalines **5b**–**m**

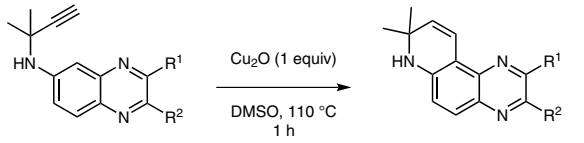



| Entry | Substrate | $R^1$ | $R^2$ | $R^3$ | Catalyst | Product | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **5b** | H | H | H | $Cu_2O$ | **6b** | 65 |
| 2 | **5c** | H | Ph | H | $Cu_2O$ | **6c** | 70 |
| 3 | **5d** | Me | Ph | H | CuCl | **6d** | 54 |
| 4 | **5e** | Me | *p*-Tol | H | CuCl | **6e** | 61 |
| 5 | **5f** | Me |  | H | CuCl | **6f** | 62 |
| 6 | **5g** | Me |  | H | CuCl | **6g** | 51 |
| 7 | **5h** | Me |  | H | CuCl | **6h** | 52 |
| 8 | **5i** | Me |  | H | CuCl | **6i** | 64 |
| 9 | **5j** | Me |  | H | CuCl | **6j** | 62 |
| 10 | **5k** | Me |  | H | CuCl | **6k** | 61 |
| 11 | **5l** | Me |  | H | CuCl | **6l** | 63 |
| 12 | **5m** | Me | H | Ph | $AgNO_3$ | **6m** | 43 |

[a] Isolated yield.

the more nucleophilic 7-position of the aniline, which gives the cyclized alkenyl metal species **B**, similar to some carbocupration when M is copper.[7] After prototropy, the metal cation is released to give 7,8-dihydro-1,4,8-triazaphenanthrene **C**, which, after hydrolysis, is spontaneously oxidized[8] to liberate the corresponding 1,4,8-triazaphenanthrene **6b**.

The regioselective 6-*endo*-dig cycloisomerization can also be performed with *N*-dimethylpropargyl-6-aminoquinoxalines **8a** and **8b**,[4e] with $Cu_2O$ for example (Scheme 3). The reaction was faster (1 h) probably because of a beneficial Thorpe–Ingold effect of the two methyl groups. In this case, no aromatization is possible and thus 7,8-dihydro-7,7-dimethyl-1,4,8-triazaphenanthrenes **9a** and **9b** were obtained in good yields.




**8a**: $R^1$ = Me, $R^2$ = H
**8b**: $R^1$ = Me, $R^2$ = Ph
**9a**: $R^1$ = Me, $R^2$ = H, 67%
**9b**: $R^1$ = Me, $R^2$ = Ph, 64%

**Scheme 3** Cyclization of quinoxalines **8a** and **8b**

In conclusion, *N*-propargyl-6-aminoquinoxaline derivatives were cyclized in a highly regioselective 6-*endo*-dig fashion to lead to the expected 1,4,8-triazaphenanthrenes and 7,8-dihydro-7,7-dimethyl-1,4,8-triazaphenanthrenes. The nature of catalyst was studied, leading to the conclusion that the metal ion must be paired with a low coordinating counteranion to give high yields. This is in agreement with our proposed mechanism, in which the metal needs to chelate the triple bond for further activation. Cuprous oxide or chloride and silver nitrate was found to be the best catalysts for the transformation, considering their reactivity and their availability as stoichiometric quantities are needed to perform this cycloisomerization. Computational calculations allowed us to rationalize the observed regioselectivity by comparing the reactivity of the positions with respect to the HOMO orbitals of the substrates, which showed that the 5-position was the more reactive in this system. The bioactivity of the newly synthesized products will be reported in due course.

All reactions involving moisture-sensitive reactants were performed under a nitrogen atmosphere using oven-dried glassware. DMSO (standard grade quality) was directly used as received. Copper, silver or gold salts were not further purified before reaction. Routine monitoring of reactions was performed using Riedel-de Haën, S, 0.063 mm, 0.032 silica gel plates, and UV detection at both 254 and 364 nm wavelength. Flash chromatography was performed using Riedel-de Haën, S, 0.063 mm, 0.032 silica under moderate pressure with the appropriate solvent giving a migrate front ($R_f$) in the range of 0.2 to 0.3.

$^1$H NMR spectra were recorded with a Bruker Avance 300 (300 MHz) and a Bruker Avance 400 (400 MHz). Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (δ = 7.26 ppm) as internal standard. $^{13}$C NMR spectra were recorded with Bruker Avance 300 (75 MHz) and Bruker Avance 400 (100 MHz) spectrometers as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (δ = 77.0 ppm) as internal standard. Some signals are broadened due to some slow conformational changes. High-resolution mass spectra (HRMS) were measured with an LCT premier spectrometer. Some low-resolution mass spectra were recorded with an HP1100 spectrometer.

### Synthesis of *N*-Propargyl 6-aminoquinoxalines 5a–m; General Procedure

To a solution of 6-aminoquinoxaline derivative **4a**–**m** (1 equiv), $K_2CO_3$ (2 equiv), and *n*-$Bu_4NI$ (0.2 equiv) in anhydrous DMF (2 mL/mmol of **4a**–**m**) under inert atmosphere was added propargyl bromide (80% in toluene, 1.5 equiv) or 3-phenyl-propargyl bromide[9] (1.5 equiv) and heated at 70 °C for 24 h. The mixture was diluted with water, extracted with EtOAc, washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel flash chromatography ($CH_2Cl_2$–EtOAc, 90:10 to 80:20) to afford monopropargyl derivatives **5a**–**m** as brownish yellow solids.

### 2-Methyl-*N*-propargyl-6-aminoquinoxaline (5a)

Yield: 2.57 g (42%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.62 (s, 1 H), 7.83 (d, *J* = 9.0 Hz, 1 H), 7.16 (dd, *J* = 9.0, 2.5 Hz, 1 H), 7.12 (d, *J* = 2.5 Hz, 1 H), 4.36 (br s, 1 H, NH), 4.10 (dd, *J* = 5.9, 2.5 Hz, 2 H), 2.72 (s, 3 H), 2.30 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 149.2, 146.6, 145.4, 142.5, 136.8, 128.9, 121.4, 105.1, 79.4, 71.5, 33.1, 21.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd $C_{12}H_{12}N_3$: 198.1031; found: 198.1023.

### *N*-Propargyl-6-aminoquinoxaline (5b)

Yield: 2.50 g (55%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.67 (d, *J* = 2.0 Hz, 1 H), 8.55 (d, *J* = 2.0 Hz, 1 H), 7.87 (d, *J* = 9.0 Hz, 1 H), 7.16 (dd, *J* = 9.0, 2.5 Hz, 1 H), 7.10 (d, *J* = 2.5 Hz, 1 H), 4.56 (br t, *J* = 5.8 Hz, 1 H, NH), 4.08 (dd, *J* = 5.8, 2.5 Hz, 2 H), 2.30 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 147.8, 145.2, 145.0, 141.1, 138.3, 130.2, 122.0, 105.1, 79.6, 72.0, 33.4.

MS (ESI): *m*/*z* = 197.0 (100) $[M + H]^+$.

### 3-Phenyl-*N*-propargyl-6-aminoquinoxaline (5c)

Yield: 290 mg (49%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 9.04 (s, 1 H), 8.15 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.90 (d, *J* = 8.5 Hz, 1 H), 7.60–7.66 (m, 3 H), 7.16 (s, 1 H), 7.15 (m, 1 H), 4.43 (br s, 1 H, NH), 4.11 (br m, 2 H), 2.29 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 152.1, 148.1, 144.4, 141.1, 139.4, 136.9, 129.9, 129.8, 129.0 (2C), 127.5 (2C), 121.5, 105.5, 79.8, 72.0, 33.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{14}N_3$: 260.1183; found: 260.1188.

### 2-Methyl-3-phenyl-*N*-propargyl-6-aminoquinoxaline (5d)

Yield: 90.1 mg (40%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.8 Hz, 1 H), 7.61 (dd, *J* = 8.8, 1.6 Hz, 2 H), 7.50 (m, 3 H), 7.43–7.12 (d, *J* = 2.6 Hz, 1 H), 7.09 (dd, *J* = 8.8, 2.6 Hz, 1 H), 4.56 (br s, 1 H, NH), 4.01 (br s, 2 H), 2.67 (s, 3 H), 2.23 (t, *J* = 2.4 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.6, 147.9, 147.3, 142.8, 139.4, 136.3, 128.9, 128.8 (2C), 128.6, 128.3 (2C), 121.6, 105.2, 79.9, 71.7, 33.3, 23.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}N_3$: 274.1344; found: 274.1342.

**2-Methyl-3-*p*-tolyl-*N*-propargyl-6-aminoquinoxaline (5e)**

Yield: 207.0 mg (40%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.9 Hz, 1 H), 7.53 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.12 (d, *J* = 2.5 Hz, 1 H), 7.10 (dd, *J* = 8.9, 2.5 Hz, 1 H), 4.48 (br s, 1 H, NH), 4.02 (br s, 2 H), 2.69 (s, 3 H), 2.42 (s, 3 H), 2.23 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.8, 148.1, 147.2, 142.9, 138.6, 136.6, 136.3, 129.1 (2C), 128.9, 128.8 (2C), 121.5, 105.4, 80.0, 71.8, 33.4, 23.8, 21.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}N_3$: 288.1501; found: 288.1501.

**2-Methyl-3-(4-methoxyphenyl)-*N*-propargyl-6-aminoquinoxaline (5f)**

Yield: 280.0 mg (71%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.7 Hz, 1 H), 7.60 (d, *J* = 8.7 Hz, 2 H), 7.12 (d, *J* = 2.5 Hz, 1 H), 7.02 (d, *J* = 8.7 Hz, 2 H), 7.09 (dd, *J* = 8.7, 2.5 Hz, 1 H), 4.44 (br s, 1 H, NH), 4.03 (d, *J* = 2.4 Hz, 2 H), 3.86 (s, 3 H), 2.70 (s, 3 H), 2.24 (t, *J* = 2.4 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 160.0, 154.4, 148.1, 147.2, 142.9, 136.1, 131.9, 130.4 (2C), 128.9, 121.4, 113.8 (2C), 105.3, 80.0, 71.8, 55.3, 33.4, 23.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{18}N_3O$: 304.1450; found: 304.1458.

**2-Methyl-3-(3,4,5-trimethoxyphenyl)-*N*-propargyl-6-aminoquinoxaline (5g)**

Yield: 118.7 mg (42%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 9.6 Hz, 1 H), 7.08–7.11 (m, 2 H), 6.80 (s, 2 H), 4.64 (br s, 1 H, NH), 4.00 (br s, 2 H), 3.87 (s, 9 H), 2.67 (s, 3 H), 2.21 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.4, 153.1 (2C), 147.7, 147.4, 142.6, 138.5, 136.3, 134.9, 128.8, 121.7, 106.2 (2C), 104.9, 79.9, 71.6, 60.8, 56.1 (2C), 33.2, 23.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}N_3O_3$: 364.1661; found: 364.1659.

**2-Methyl-3-(4-fluorophenyl)-*N*-propargyl-6-aminoquinoxaline (5h)**

Yield: 74.0 mg (28%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 9.2 Hz, 2 H), 7.64 (dd, *J* = 8.8, 5.6 Hz, 1 H), 7.51 (dd, *J* = 9.2, 2.7 Hz, 1 H), 7.42 (d, *J* = 2.7 Hz, 1 H), 7.20 (t, *J* = 8.8 Hz, 2 H), 4.27 (s, 1 H, NH), 4.27 (d, *J* = 2.5 Hz, 2 H), 2.71 (s, 3 H), 2.26 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 163.1 (d, $J_{C-F}$ = 248.0 Hz), 154.0, 148.8, 148.2, 142.9, 136.5, 135.6 (d, $J_{C-F}$ = 2.0 Hz), 130.9 (d, $J_{C-F}$ = 8.5 Hz, 2C), 128.9, 121.8, 115.5 (d, $J_{C-F}$ = 22.4 Hz, 2C), 109.9, 80.0, 73.1, 40.4, 23.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}N_3F$: 292.1250; found: 292.1250.

**2-Methyl-3-(4-chlorophenyl)-*N*-propargyl-6-aminoquinoxaline (5i)**

Yield: 160.0 mg (34%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.7 Hz, 1 H), 7.58 (d, *J* = 8.4 Hz, 2 H), 7.48 (d, *J* = 8.4 Hz, 2 H), 7.13 (dd, *J* = 8.7, 2.5 Hz, 1 H), 4.10 (d, *J* = 2.5 Hz, 1 H), 7.44 (br s, 1 H, NH), 4.05 (br s, 2 H), 2.68 (s, 3 H), 2.25 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.5, 147.7, 147.4, 142.9, 137.9, 136.5, 134.9, 130.3 (2C), 129.1, 128.7 (2C), 121.9, 105.2, 79.9, 71.9, 33.4, 23.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}ClN_3$: 308.0955; found: 308.0959.

**2-Methyl-3-(3,4-dichlorophenyl)-*N*-propargyl-6-aminoquinoxaline (5j)**

Yield: 196.0 mg (50%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 9.0 Hz, 1 H), 7.77 (d, *J* = 2.0 Hz, 1 H), 7.59 (d, *J* = 8.2 Hz, 1 H), 7.49 (dd, *J* = 8.2, 2.0 Hz, 1 H), 7.17 (dd, *J* = 9.0, 2.5 Hz, 1 H), 7.10 (d, *J* = 2.5 Hz, 1 H), 4.40 (t, *J* = 5.7 Hz, 1 H, NH), 4.07 (dd, *J* = 5.7, 2.5 Hz, 2 H), 2.70 (s, 3 H), 2.27 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 152.1, 147.5, 147.4, 142.9, 139.4, 136.8, 133.1, 132.8, 131.1, 130.4, 129.2, 128.3, 122.3, 105.1, 79.8, 72.0, 33.5, 23.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}Cl_2N_3$: 342.0565; found: 342.0565.

**2-Methyl-3-(naphthalen-2-yl)-*N*-propargyl-6-aminoquinoxaline (5k)**

Yield: 80.5 mg (28%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.97 (d, *J* = 8.4 Hz, 1 H), 7.92 (t, *J* = 4.7 Hz, 2 H), 7.86 (d, *J* = 8.5 Hz, 1 H), 7.75 (dd, *J* = 8.5, 1.7 Hz, 1 H), 7.51–7.57 (m, 2 H), 7.17 (d, *J* = 2.5 Hz, 1 H), 7.12 (dd, *J* = 9.0, 2.5 Hz, 1 H), 4.48 (t, *J* = 5.5 Hz, 1 H), 4.04 (dd, *J* = 5.5, 2.5 Hz, 2 H), 2.74 (s, 3 H), 2.25 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 154.6, 148.1, 147.3, 142.9, 136.8, 136.4, 133.1, 133.0, 129.0, 128.5, 128.4, 128.1, 127.7, 126.6, 126.4 (2C), 121.7, 105.3, 79.9, 71.8, 33.4, 23.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{18}N_3$: 324.1501; found: 324.1472.

**2-Methyl-3-biphenyl-*N*-propargyl-6-aminoquinoxaline (5l)**

Yield: 80.4 mg (23%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.9 Hz, 1 H), 7.73 (s, 4 H), 7.67 (dd, *J* = 7.4, 1.9 Hz, 2 H), 7.48 (t, *J* = 7.4 Hz, 2 H), 7.38 (tt, *J* = 7.4, 1.9 Hz, 1 H), 7.16 (d, *J* = 2.7 Hz, 1 H), 7.14 (dd, *J* = 8.9, 2.7 Hz, 1 H), 4.40 (br s, 1 H, NH), 4.06 (d, *J* = 2.5 Hz, 2 H), 2.76 (s, 3 H), 2.26 (t, *J* = 2.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.4, 148.1, 147.3, 143.0, 141.6, 140.6, 138.4, 136.4, 129.4 (2C), 129.0, 128.8 (2C), 127.6, 127.2 (4C), 121.7, 105.4, 80.0, 71.9, 33.5, 23.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{18}N_3$: 348.1501; found: 348.1499.

**2-Methyl-5-phenyl-*N*-propargyl-6-aminoquinoxaline (5m)**

Yield: 30.4 mg (31%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 7.80 (d, *J* = 9.0 Hz, 1 H), 7.42–7.36 (m, 2 H), 7.30–7.25 (m, 3 H), 7.17 (dd, *J* = 9.0, 2.5 Hz, 2 H), 7.13 (d, *J* = 2.5 Hz, 1 H), 4.52 (br s, 1 H, NH), 4.27 (d, *J* = 4.6 Hz, 2 H), 2.67 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 149.4, 147.3, 145.8, 143.0, 137.2, 131.7, 129.3, 128.3, 128.2, 122.6, 121.8, 105.5, 85.2, 83.8, 34.4, 22.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}N_3$: 274.1344; found: 272.1341.

**Synthesis of*N*-(1,1-Dimethyl)propargyl-6-aminoquinoxalines 8a,b; General Procedure**

To a solution of aminoquinoxaline **4a**,**b** (1 equiv) in a 1:1 mixture of THF/water (10 mL / 10 mL) with $CuCl_2$, (10 mg/mmol) and copper dust (10 mg/mmol) under an inert atmosphere, was added triethylamine (1.4 equiv) and 3-chloro-3-methyl-1-butyne[10] (1.4 equiv). The mixture was stirred at r.t. for 12 h, hydrolyzed with sat. aq $K_2CO_3$, and then extracted with $CH_2Cl_2$. The combined organic layers were washed with sat. aq NaCl, dried over $Na_2SO_4$, filtered then concentrated in vacuo. The residue was then purified by flash chromatography ($CH_2Cl_2$–EtOAc, 90:10 to 80:20) to afford the expected compound **8a**,**b**.

**2-Methyl-*N*-(1,1-dimethyl)-propargyl-6-aminoquinoxaline (8a)**

Yield: 224 mg (80%); brownish yellow solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.47 (s, 1 H), 7.66 (d, *J* = 9.0 Hz, 1 H), 7.46 (d, *J* = 2.5 Hz, 1 H), 7.10 (dd, *J* = 9.0, 2.5 Hz, 1 H, $H_7$), 4.59 (br s, 1 H, NH), 2.55 (s, 3 H), 2.35 (s, 1 H), 1.57 (s, 6 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 149.0, 145.6, 145.4, 142.4, 136.6, 128.6, 123.2, 107.7, 86.3, 71.2, 47.6, 29.8, 21.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}N_3$: 226.1344; found: 226.1341.

**2-Methyl-3-phenyl-*N*-(1,1-dimethyl)-propargyl-6-aminoquinoxaline (8b)**

Yield: 414.0 mg (65%); brownish yellow solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 9.0 Hz, 1 H), 7.61 (d, *J* = 8.3 Hz, 2 H), 7.56 (d, *J* = 2.5 Hz, 1 H), 7.41–7.50 (m, 3 H), 7.16 (dd, *J* = 9.0, 2.5 Hz, 1 H), 4.32 (br s, 1 H, NH), 2.66 (s, 3 H), 2.40 (s, 1 H), 1.68 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 154.6, 147.8, 145.8, 142.6, 139.6, 136.1, 128.8 (2C), 128.6, 128.5, 128.4 (2C), 123.2, 108.0, 86.4, 71.2, 47.8, 30.0 (2C), 23.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}N_3$: 302.1657; found: 302.1656.

**Synthesis of 1,4,8-Triazaphenanthrene 6a–m and 7,8-Dihydro-7,7-dimethyl-1,4,8-triazaphenanthrenes 9a,b**

To a solution of *N*-propargyl-6-aminoquinoxaline derivative **5a**–**m** or **8a,b** (1 equiv) in DMSO (10 mL/mmol of **5a**–**m**) was added the corresponding copper or silver catalyst (see Table 2) under an inert atmosphere. The resulting solution was stirred for 5 h at 110 °C. The reaction mixture was cooled to r.t., $NH_4OH$ 28% (1 mL/mmol) was added, and the reaction mixture was stirred for 10 min at r.t., then diluted with water, extracted with EtOAc twice, washed with sat. aq NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The mixture was purified by silica gel flash chromatography ($CH_2Cl_2$–EtOAc, 90:10 to 80:20) to afford **6a**–**m** or **9a,b**.

**2-Methyl-1,4,8-triazaphenanthrene (6a)**

Yield and catalysts: see Table 1; light-beige solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 9.44 (dd, *J* = 8.3, 1.7 Hz, 1 H), 9.07 (dd, *J* = 4.4, 1.7 Hz, 1 H, H-13), 8.83 (s, 1 H), 8.28 (d, *J* = 9.47 Hz, 1 H, H-7), 8.16 (d, *J* = 9.4 Hz, 1 H, H-8), 7.66 (dd, *J* = 9.4, 4.4 Hz, 1 H, H-12), 2.83 (s, 3 H, $CH_3$).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 154.1, 151.3, 148.5, 144.3, 141.1, 138.2, 132.7, 132.2, 130.1, 126.2, 122.1, 22.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{10}N_3$: 196.0875; found: 196.0873.

**1,4,8-Triazaphenanthrene (6b)**

Yield: 91 mg (70%); light-beige solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 9.44 (ddd, *J* = 8.2, 1.7, 0.5 Hz, 1 H), 9.01 (dd, *J* = 4.4, 1.7 Hz, 1 H), 8.94 (d, *J* = 2.0 Hz, 1 H), 8.92 (d, *J* = 2.0 Hz, 1 H), 8.28 (d, *J* = 9.2 Hz, 1 H), 8.17 (d, *J* = 9.2 Hz, 1 H), 7.65 (dd, *J* = 8.2, 4.4 Hz, 1 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 151.9, 149.1, 145.1, 143.8, 142.4, 140.9, 133.1, 132.7, 130.5, 126.4, 122.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_8N_3$: 182.0718; found: 182.0717.

**3-Phenyl-1,4,8-triazaphenanthrene (6c)**

Yield: 163 mg (70%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.66 (d, *J* = 8.3 Hz, 1 H), 9.46 (s, 1 H), 9.15 (br s, 1 H), 8.33 (dd, *J* = 8.3, 1.5 Hz, 2 H), 8.26 (t, *J* = 8.5 Hz, 2 H), 7.72 (br m, 1 H), 7.61 (m, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 151.9 (br), 150.7, 149.7 (br), 142.9, 140.7, 140.1, 136.5, 132.8, 132.4, 130.3, 130.2, 129.2 (2C), 127.5 (2C), 126.8 (br), 122.3 (br).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{12}N_3$: 258.1031; found: 258.1028.

**2-Methyl-3-phenyl-1,4,8-triazaphenanthrene (6d)**

Yield: 33.9 mg (54%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.42 (dd, *J* = 8.3, 0.8 Hz, 1 H), 9.03 (br s, 1 H), 8.23 (d, *J* = 9.2 Hz, 1 H), 8.12 (d, *J* = 9.2 Hz, 1 H), 7.76 (dd, *J* = 8.1, 1.5 Hz, 2 H), 7.48–7.59 (m, 4 H), 2.84 (s, 3 H); some signals are broadened due to slow conformational changes.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.2, 152.4, 151.3 (br), 148.8 (br), 139.9, 138.8, 138.1, 132.5, 132.4, 129.7, 129.3 (2C), 129.0, 128.4 (2C), 126.4 (br), 122.0 (br), 24.1; some signals are broadened due to slow conformational changes.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}N_3$: 272.1188; found: 272.1183.

**2-Methyl-3-*p*-tolyl-1,4,8-triazaphenanthrene (6e)**

Yield: 30.5 mg (61%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.46 (dd, *J* = 8.2, 1.0 Hz, 1 H), 9.03 (dd, *J* = 4.4, 1.8 Hz, 1 H), 8.24 (d, *J* = 9.2 Hz, 1 H), 8.15 (d, *J* = 9.2 Hz, 1 H), 7.68 (d, *J* = 8.2 Hz, 2 H), 7.59 (dd, *J* = 8.2, 4.4 Hz, 1 H), 7.36 (d, *J* = 8.2 Hz, 2 H), 2.87 (s, 3 H), 2.47 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.3, 152.5, 151.3, 148.9, 139.9, 139.1, 138.2, 136.1, 132.5, 132.2, 129.8, 129.3 (2C), 129.1 (2C), 126.4, 122.0, 24.2, 21.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{16}N_3$: 286.1344; found: 286.1344.

**2-Methyl-3-(4-methoxyphenyl)-1,4,8-triazaphenanthrene (6f)**

Yield: 30.2 mg (62%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.45 (dd, *J*= 8.0, 0.8 Hz, 1 H), 9.03 (br s, 1 H), 8.23 (d, *J* = 9.3 Hz, 1 H), 8.12 (d, *J* = 9.3 Hz, 1 H), 7.75 (dd, *J* = 8.8, 2.0 Hz, 2 H), 7.59 (dd, *J* = 8.0, 4.1 Hz, 1 H), 7.07 ( d, *J* = 8.8 Hz, 2 H), 3.90 (s, 3 H), 2.87 (s, 3 H); some signals are broadened due to slow conformational changes.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 160.4, 152.8, 152.4, 151.2 (br), 148.9 (br), 139.7, 138.2, 132.5, 132.1, 131.2, 130.8 (2C), 129.8, 126.4 (br), 122.0 (br), 113.9 (2C), 55.4, 24.4; some signals are broadened due to slow conformational changes.

MS (ESI): *m*/*z* = 302.2 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{16}N_3O$: 302.1293; found: 302.1296.

**2-Methyl-3-(3,4,5-trimethoxyphenyl)-1,4,8-triazaphenanthrene (6g)**

Yield: 25.2 mg (51%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.47 (d, *J*= 8.0 Hz, 1 H), 9.06 (br s, 1 H), 8.26 (d, *J* = 9.3 Hz, 1 H), 8.16 (d, *J* = 9.3 Hz, 1 H), 7.63 (dd, *J* = 8.0, 3.9 Hz, 1 H), 6.98 (s, 2 H), 3.95 (s, 9 H), 2.88 (s, 3 H); some signals are broadened due to slow conformational changes.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.3 (2C), 153.1, 152.5, 151.4 (br), 149.0 (br), 140.1, 138.8, 138.0, 134.3, 132.5 (2C), 129.8, 126.3 (br), 122.1 (br), 106.8 (2C), 61.0, 56.4 (2C), 24.3; some signals are broadened due to slow conformational changes.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}N_3O_3$: 362.1505; found: 362.1503.

**2-Methyl-3-(4-fluorophenyl)-1,4,8-triazaphenanthrene (6h)**

Yield: 52% (19.0 mg); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.46 (dd, *J* = 8.0, 1.5 Hz, 1 H), 9.07 (d, *J* = 3.0 Hz, 1 H), 8.26 (d, *J* = 9.3 Hz, 1 H), 8.15 (d, *J* = 9.3 Hz, 1 H), 7.78 (dd, *J* = 8.5, 5.0 Hz, 2 H), 7.62 (dd, *J* = 8.3, 4.2 Hz, 1 H), 7.27 (t, *J* = 8.5 Hz, 2 H), 2.88 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 163.3 (d, $J_{C-F}$ = 250.8 Hz), 152.3, 152.2, 151.5, 148.9, 140.1, 138.2, 135.0 (d, $J_{C-F}$ = 3.1 Hz), 132.6, 132.5, 131.3 (d, $J_{C-F}$ = 8.0 Hz, 2C), 129.8, 126.3, 122.1, 115.5 (d, $J_{C-F}$ = 21.5 Hz, 2C), 24.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{13}N_3F$: 290.1094; found: 290.1094.

**2-Methyl-3-(4-chlorophenyl)-1,4,8-triazaphenanthrene (6i)**

Yield: 30.4 mg (64%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.47 (d, *J* = 8.3 Hz, 1 H), 9.10 (br s, 1 H), 8.29 (br d, *J* = 8.4 Hz, 1 H), 8.17 (d, *J* = 8.4 Hz, 1 H), 7.74 (d, *J* = 8.2 Hz, 2 H), 7.66 (br s, 1 H), 7.55 (d, *J* = 8.2 Hz, 2 H), 2.87 (s, 3 H); some signals are broadened due to slow conformational changes.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 152.3, 152.1, 151.4 (br), 149.2 (br), 140.3, 138.3, 137.4, 135.4, 132.9 (br), 132.5, 130.8 (2C), 129.8, 128.8 (2C), 125.7 (br), 122.4 (br), 24.1; some signals are broadened due to slow conformational changes.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{13}ClN_3$: 306.0798; found: 306.0800.

**2-Methyl-3-(3,4-dichlorophenyl)-1,4,8-triazaphenanthrene (6j)**

Yield: 34.6 mg (62%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.46 (dd, *J* = 8.3, 1.4 Hz, 1 H), 9.08 (br s, 1 H), 8.30 (d, *J* = 9.3 Hz, 1 H), 8.17 (d, *J* = 9.3 Hz, 1 H), 7.91 (d, *J* = 1.0 Hz, 1 H), 7.61–7.67 (m, 3 H), 2.88 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 152.1, 151.7, 150.7, 149.0, 140.5, 138.8, 138.3, 133.6, 133.2, 132.9, 132.5, 131.4, 130.5, 129.8, 128.6, 126.3, 122.3, 24.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{12}Cl_2N_3$: 340.0408; found: 340.0405.

**2-Methyl-3-(naphthalen-2-yl)-1,4,8-triazaphenanthrene (6k)**

Yield: 30.1 mg (61%).; light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.57 (d, *J* = 6.6 Hz, 1 H), 9.17 (br s, 1 H), 8.35 (br s, 1 H), 8.26 (s, 1 H), 8.24 (br s, 1 H), 8.01 (d, *J* = 8.6 Hz, 1 H), 7.98 (dd, *J* = 6.4, 5.0 Hz, 1 H), 7.96 (dd, *J* = 6.4, 5.0 Hz, 1 H), 7.91 (dd, *J* = 8.5, 1.5 Hz, 1 H), 7.74 (m, 1 H), 7.60 (m, 2 H), 2.95 (s, 3 H); some signals are broadened due to slow conformational changes.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.4, 152.8, 140.2, 136.3, 135.9, 132.4, 133.4, 133.0, 132.6 (br), 129.8 (br), 129.1, 128.5, 128.2, 127.8, 127.0, 126.7, 126.7, 24.3; some signals are broadened and 4 C missing due to slow conformational change.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{16}N_3$: 322.1344; found: 322.1344.

**2-Methyl-3-biphenyl-1,4,8-triazaphenanthrene (6l)**

Yield: 34.5 mg (63%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.52 (dd, *J* = 8.2, 1.3 Hz, 1 H), 9.07 (dd, *J* = 4.5, 1.8 Hz, 1 H), 8.29 (d, *J* = 9.3 Hz, 1 H), 8.19 (d, *J* = 9.3 Hz, 1 H), 7.89 (dd, *J* = 8.6, 1.9 Hz, 2 H), 7.80 (dd, *J* = 8.6, 1.9 Hz, 2 H), 7.70 (d, *J* = 7.1 Hz, 2 H), 7.64 (dd, *J* = 8.2, 4.5 Hz, 1 H), 7.51 (td, *J* = 7.3, 1.9 Hz, 2 H), 7.41 (tt, *J* = 7.3, 1.9 Hz, 1 H), 2.94 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 152.9, 152.6, 151.5, 149.0, 142.0, 140.4, 140.1, 138.3, 137.8, 132.6, 132.5, 129.9 (3C), 128.9 (2C), 127.8, 127.2 (4C), 126.5, 122.1, 24.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{18}N_3$: 348.1501; found: 348.1499.

**2-Methyl-5-phenyl-1,4,8-triazaphenanthrene (6m)**

Reaction time: 1 h.

Yield: 86.0 mg (43%); light-beige solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 9.01 (d, *J* = 4.7 Hz, 1 H), 8.34 (d, *J* = 8.9 Hz, 1 H), 8.32 (s, 1 H), 8.14 (d, *J* = 8.9 Hz, 1 H), 7.44 (d, *J* = 4.7 Hz, 1 H), 7.43–7.39 (m, 3 H), 7.36–7.30 (m, 2 H), 2.68 (s, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 153.1, 150.1, 149.91, 149.8, 142.6, 142.3, 141.7, 139.1, 133.4, 128.1 (2C), 127.7 (2C), 127.1, 125.4, 124.1, 22.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}N_3$: 272.1188; found: 272.1178.

**7,8-Dihydro-2,8,8-trimethylpyrido[3,2-*f*]quinoxaline (9a)**

Reaction time: 1 h.

Yield: 67 mg (67%); light-beige solid.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.51 (s, 1 H), 7.59 (d, *J* = 9.0 Hz, 1 H), 7.33 (d, *J* = 10.0 Hz, 1 H), 6.92 (d, *J* = 9.0 Hz), 5.55 (d, *J* = 10.12 Hz, 1 H), 4.16 (br s, 1 H, NH), 2.63 (s, 3 H), 1.36 (s, 6 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 148.6, 145.0, 142.9, 138.3, 136.6, 129.0, 128.3, 120.1, 118.4, 111.5, 52.6, 31.4 (2C), 21.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}N_3$: 226.1344; found: 226.1349.

**7,8-Dihydro-2,8,8-trimethyl-3-phenylpyrido[3,2-*f*]quinoxaline (9b)**

Reaction time: 1 h.

Yield: 191.0 mg (64%); light-beige solid.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.70 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.65 (d, *J* = 8.8 Hz, 1 H), 7.45–7.52 (m, 3 H), 7.42 (d, *J* = 9.8 Hz, 1 H), 6.93 (d, *J* = 8.8 Hz, 1 H), 5.52 (d, *J* = 9.8 Hz, 1 H), 4.07 (br s, NH, 1 H), 2.69 (s, 3 H), 1.38 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 153.7, 147.0, 143.0, 139.9, 138.3, 135.7, 129.2 (2C), 128.7, 128.6, 128.2 (2C), 128.0, 119.9, 118.8, 111.7, 52.6, 31.4 (2C), 23.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}N_3$: 302.1657; found: 302.1650.

### Computational Methods

The conformation of a model of derivative **5b** was fully optimized without constraint by using the DFT[11] method with the hybrid Becke3LYP functional[12] and the 6–31G* base[13] as implemented in the Gaussian 09 software package.[14] Vibrational analysis within the harmonic approximation was performed at the same level of theory upon geometrical optimization convergence, and the local minimum was characterized by the absence of an imaginary frequency. Depiction of the molecular geometry as well as orbitals was realized by using UCSF Chimera v1.10.2.[15]

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## Supporting Information

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