A New Practical Approach Towards the Synthesis of Unsymmetric and Symmetric 1,10-Phenanthroline Derivatives at Room Temperature

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Materials and Methods

8-aminoquinoline was purchased from Aladdin and purified by column chromatography, other commercial materials (Alfa Aesar, Aladdin, J&K Chemical LTD., Beijing Ouhe Technology Co., Ltd.) were used without further purification. All solvents were analytical grade. CH$_2$Cl$_2$, MeCN, MeOH, PhMe, DMSO and ClCH$_2$CH$_2$Cl were dried according to the procedure described in the fifth edition of "Purification of Laboratory Chemicals" by W.L.F. Armarego & C.L.L. Chai.\(^1\)

The $^1$H NMR and $^{13}$C NMR spectra were recorded on a JOEL JNM-ECA 300 MHz or BRUKE AVANCE 400 MHz spectrometer in CDCl$_3$ using TMS or solvent peak as a standard. All $^{13}$C NMR spectra were recorded with complete proton decoupling. Low-resolution mass spectral analyses were performed with a Waters AQUITY UPLC$^{\text{TM}}$/MS. Analytical TLC was performed on Yantai Chemical Industry Research Institute silica gel 60 F254 plates and flash column chromatography was performed on Qingdao Haiyang Chemical Co., Ltd silica gel 60 (200-300mesh). The rotavapor was BUCHI’s Rotavapor R-3. Substituted 3-ethoxycyclobutanones\(^2,[3]\) and 2-azidoaniline\(^4\) was prepared according to the literature reports.

General procedure

I Synthesis of substituted 8- aminoquinolines

2-azidoaniline (1.0 equiv) and substituted 3-ethoxycyclobutanones (2.0 equiv) were dissolved in anhydrous dichloromethane in a flame-dried round bottom flask which was coated with aluminum foil. Following that, BF$_3$·OEt$_2$ (1.0 equiv) was added into the reaction solution. Then the reaction mixture was stirred at room temperature under atmosphere of Argon for 6 - 12 h. The reaction was monitored by TLC and LC-MS. After completion of the reaction, Et$_3$N was added to quench the reaction. The reaction mixture was diluted with dichloromethane and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally the residue was purified by silical gel column chromatography to give substituted 8-azidoquinoline, then the substituted 8-azidoquinolines were added to a solution of triphenylphosphine in anhydrous methanol. The flask was also coated with aluminum foil. Then, the reaction was stirred at 50°C overnight. After all the starting material had disappeared, the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was purified by silical gel column chromatography to give corresponding substituted 8-aminoquinolines.

II Synthesis of 1,10-phenanthrolines

8-aminoquinoline or substituted 8-aminoquinolines (prepared by following the general procedure I) (1.0 equiv) and substituted 3-ethoxycyclobutanones (2.0 equiv) were dissolved in anhydrous dichloromethane in a flame-dried round bottom flask. Following that, crushed 4 Å molecular sieves (150%wt) was added quickly, then BF$_3$·OEt$_2$ (1.0 equiv) was dropwised into the reaction solution. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48 h. The reaction was monitored by TLC and LC-MS. After 48h, Et$_3$N was added to quench the reaction. The reaction mixture was diluted with dichloromethane and filtered through SiO$_2$ then washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 2 : 1, then DCM : MeOH = 80 : 1) to give corresponding 1,10-phenanthroline.
References:

2-cyclopentyl-1,10-phenanthroline (3)
Following the general procedure II, 3-ethoxy-spiro[3.4]octan-1-one (47 mg, 0.28 mmol), 8-aminoquinoline (20 mg, 0.14 mmol), BF$_3$·OEt$_2$ (1.0 equiv, 0.14 mmol) and crushed 4 Å molecular sieves (150\%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 3 (30 mg, colorless oil) was isolated in 87\% yield.$^1$H-NMR (300 MHz, CDCl$_3$) δ (ppm) 9.21 (dd, $J$ = 1.59 Hz, $J$ = 4.32 Hz, 1H), 8.23 (dd, $J$ = 1.62 Hz, $J$ = 8.04 Hz, 1H), 8.17 (d, $J$ = 8.37 Hz, 1H), 7.76 (d, $J$ = 8.76 Hz, 1H), 7.72 (d, $J$ = 8.76 Hz, 1H), 7.61 - 7.57 (m, 2H), 3.78 - 3.73 (m, 1H), 2.35 - 2.31 (m, 2H), 1.91 - 1.82 (m, 6H);
$^{13}$C-NMR (75 MHz, CDCl$_3$) δ (ppm) 167.4, 150.4, 146.2, 145.3, 136.5, 136.1, 128.9, 127.1, 126.5, 125.6, 122.7, 120.9, 49.5, 34.8, 26.3; MS (ESI) calcd for C$_{17}$H$_{16}$N$_2$ [M+H]$^+$: 249.13, found 249.07

2-ethyl-1,10-phenanthroline (4)
Following the general procedure II, 3-ethoxy-2-methylcyclobutanone (70 mg, 0.54 mmol), 8-aminoquinoline (39 mg, 0.27 mmol), BF$_3$·OEt$_2$ (1.0 equiv, 0.27 mmol) and crushed 4 Å molecular sieves (150\%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 4 (43 mg, colorless oil) was isolated in 76\% yield.$^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.30 (d, $J$ = 1.59 Hz, $J$ = 4.32 Hz, 1H), 8.32 (dd, $J$ = 8.12 Hz, 1H), 8.22 (d, $J$ = 8.24 Hz, 1H), 7.83 (dd, $J$ = 8.04 Hz, 1H), 7.68 (d, $J$ = 8.24 Hz, 1H), 6.62 (d, $J$ = 8.24 Hz, 1H), 3.25 (q, $J$ = 7.64 Hz, 2H), 1.46 (t, $J$ = 7.64 Hz, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 164.7, 150.1, 145.8, 145.4, 136.1, 128.9, 127.1, 126.5, 125.6, 122.7, 120.9, 49.5, 34.8, 26.3; MS (ESI) calcd for C$_{14}$H$_{12}$N$_2$ [M+H]$^+$: 209.10, found 209.00
2-propyl-1,10-phenanthroline (5)
Following the general procedure II, 3-ethoxy-2-ethylcyclobutanone (30 mg, 0.21 mmol), 8-aminoquinoline (15 mg, 0.10 mmol), BF₃·OEt₂ (1.0 equiv, 0.10 mmol) and crushed 4 Å molecular sieves (150% wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48 h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 5 (19 mg, colorless oil) was isolated in 82% yield.¹H-NMR (300 MHz, CDCl₃) δ (ppm) 9.22 (d, J = 4.38 Hz, 1H), 8.23 (d, J = 8.04 Hz, 1H), 8.16 (d, J = 8.16 Hz, 1H), 7.77 (d, J = 8.82 Hz, 1H), 7.72 (d, J = 8.73 Hz, 1H), 7.60 (dd, J = 4.29 Hz, J = 7.92 Hz, 1H), 7.54 (d, J = 8.22 Hz, 1H) 3.19 (t, J = 7.56 Hz, 2H), 1.93 - 1.89 (m, 2H), 1.08 (t, J = 8.04 Hz, 1H), 8.16 (d, J = 8.22 Hz, 1H), 7.64 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.38 - 7.32 (m, 5H), 7.25 (t, J = 6.54 Hz, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ (ppm) 163.6, 150.4, 146.2, 145.9, 136.3, 136.1, 128.9, 127.0, 126.6, 125.6, 122.9, 122.7, 41.6, 23.8, 14.2; MS (ESI) calcd for C₁₅H₁₄N₂ [M+H]+: 223.12, found 223.00

2-benzyl-1,10-phenanthroline (6)
Following the general procedure II, 3-ethoxy-2-phenylcyclobutanone (66 mg, 0.35 mmol), 8-aminoquinoline (25 mg, 0.17 mmol), BF₃·OEt₂ (1.0 equiv, 0.17 mmol) and crushed 4 Å molecular sieves (150% wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48 h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 6 (40 mg, yellow oil) was isolated in 85% yield.¹H-NMR (400 MHz, CDCl₃) δ (ppm) 9.27 (dd, J = 1.64 Hz, J = 4.36 Hz, 1H), 8.26 (dd, J = 1.04 Hz, J = 8.04 Hz, 1H), 8.10 (d, J = 8.28 Hz, 1H), 7.75 (s, 2H), 7.64 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.38 - 7.32 (m, 5H), 7.25 (t, J = 7.00 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 162.2, 150.1, 145.7, 145.3, 139.5, 136.5, 129.6, 128.9, 128.7, 127.1, 126.6, 126.5, 125.8, 123.3, 122.9, 45.7; MS (ESI) calcd for C₁₅H₁₄N₂ [M+H]+: 271.12, found 271.02

2-phenethyl-1,10-phenanthroline (7)
Following the general procedure II, 3-ethoxy-2-benzylcyclobutanone (71 mg, 0.35 mmol), 8-aminoquinoline (33 mg, yellow oil) was isolated in 67% yield.¹H-NMR (400 MHz, CDCl₃) δ (ppm) 9.24 (dd, J = 1.72 Hz, J =
4.36 Hz, 1H), 8.24 (dd, J = 1.56 Hz, J = 7.76 Hz, 1H), 8.13 (d, J = 8.20 Hz, 1H), 7.77 (d, J = 8.76 Hz, 1H), 7.74 (d, J = 8.76 Hz, 1H), 7.62 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.46 (d, J = 8.20 Hz, 1H), 7.30 - 7.29 (m, 4H), 7.23 - 7.21 (m, 1H), 3.57 - 3.53 (m, 2H), 3.26 - 3.22 (m, 2H); 1H-NMR (100 MHz, CDCl3) δ (ppm) 158.3, 150.4, 146.2, 145.6, 136.4, 136.1, 131.7, 130.6, 128.9, 127.0, 126.5, 125.8, 123.1, 122.8, 114.1, 55.3, 44.8; MS (ESI) calcd for C20H16N2 [M+H]+: 285.13, found 285.02

![Image of 2-isopropyl-1,10-phenanthroline](image1)

**2-isopropyl-1,10-phenanthroline (8)**

Following the general procedure II, 3-ethoxy-2,2-dimethylcyclobutanone (49 mg, 0.35 mmol), 8-aminoquinoline (25 mg, 0.17 mmol), BF3 OEt2 (1.0 equiv, 0.17 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 8 (29 mg, colorless oil) was isolated in 75% yield. 1H-NMR (400 MHz, CDCl3) δ (ppm) 9.20 - 9.18 (m, J = 1H), 8.16 - 8.12 (m, 2H), 7.70 - 7.63 (m, 2H), 7.56 - 7.52 (m, 2H), 3.68 - 3.61 (m, 1H), 1.43 (d, J = 6.96 Hz, 6H); 13C-NMR (100 MHz, CDCl3) δ (ppm) 168.5, 150.2, 146.2, 145.3, 136.6, 135.9, 128.8, 127.1, 126.4, 125.5, 122.6, 120.0, 37.7, 23.2; MS (ESI) calcd for C18H14N2 [M+H]+: 223.12, found 223.03

![Image of 2-(4-methoxybenzyl)-1,10-phenanthroline](image2)

**2-(4-methoxybenzyl)-1,10-phenanthroline (9)**

Following the general procedure II, 3-ethoxy-2-(4-methoxy-phenyl)-cyclobutanone (122 mg, 0.56 mmol), 8-aminoquinoline (40 mg, 0.28 mmol), BF3 OEt2 (1.0 equiv, 0.28 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 9 (62 mg, slight yellow oil) was isolated in 74% yield. 1H-NMR (400 MHz, CDCl3) δ (ppm) 9.27 (dd, J = 1.76 Hz, J = 4.36 Hz, 1H), 8.27 (dd, J = 1.76 Hz, J = 8.04 Hz, 1H), 8.12 (d, J = 8.20 Hz, 1H), 7.77 (s, 2H), 7.65 (dd, J = 4.36 Hz, J = 8.08 Hz, 1H), 7.38 (d, J = 8.32 Hz, 1H), 7.29 (d, J = 8.92 Hz, 2H), 6.89 (d, J = 8.68 Hz, 2H), 4.61 (s, 2H), 3.82 (s, 3H); 13C-NMR (100 MHz, CDCl3) δ (ppm) 162.5, 158.3, 150.4, 146.2, 145.6, 136.4, 136.1, 131.7, 130.6, 128.9, 127.0, 126.5, 125.8, 123.1, 122.8, 114.1, 55.3, 44.8; MS (ESI) calcd for C20H16O2 [M+H]+: 301.13, found 301.19
2-(2-methylbenzyl)-1,10-phenanthroline (10)
Following the general procedure II, 3-ethoxy-2-o-tolyl-cyclobutanone (113 mg, 0.56 mmol), 8-aminoquinoline (40 mg, 0.28 mmol), BF₃·OEt₂ (1.0 equiv, 0.28 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 10 (60 mg, slight yellow oil) was isolated in 76% yield. ¹H-NMR (400 MHz, CDCl₃) δ (ppm) 9.17 (dd, J = 1.76 Hz, J = 4.36 Hz, 1H), 8.09 (dd, J = 1.76 Hz, J = 8.08 Hz, 1H), 7.93 (d, J = 8.28 Hz, 1H), 7.59 (s, 2H), 7.50 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.17 - 7.09 (m, 6H), 4.62 (s, 2H), 2.22 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 161.7, 150.3, 146.1, 145.7, 137.5, 136.5, 136.0, 130.5, 128.8, 126.9, 126.4, 126.2, 125.7, 122.3, 43.5, 19.9; MS (ESI) calcd for C₂₀H₁₆N₂ [M+H]⁺: 285.13, found 285.12

2-cyclohexyl-1,10-phenanthroline (11)
Following the general procedure II, 3-ethoxy-spiro[3.5]nonan-1-one (38 mg, 0.21 mmol), 8-aminoquinoline (15 mg, 0.10 mmol), BF₃·OEt₂ (1.0 equiv, 0.10 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 11 (18 mg, colorless oil) was isolated in 66% yield. ¹H-NMR (400 MHz, CDCl₃) δ (ppm) 9.25 (dd, J = 1.76 Hz, J = 4.36 Hz, 1H), 8.25 (dd, J = 1.52 Hz, J = 8.04 Hz, 1H), 8.20 (d, J = 8.32 Hz, 1H), 7.78 (d, J = 8.76 Hz, 1H), 7.74 (d, J = 8.72 Hz, 1H), 7.62 (dd, J = 4.36 Hz, J = 8.00 Hz, 1H), 7.60 (d, J = 8.36 Hz, 1H), 3.40 - 3.34 (m, 1H), 2.17 - 2.13 (m, 2H), 1.93 - 1.89 (m, 2H), 1.86 - 1.59 (m, 2H), 1.58 - 1.48 (m, 2H), 1.42 - 1.36 (m, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 167.6, 150.4, 146.3, 145.5, 136.5, 136.0, 128.8, 127.2, 126.5, 125.5, 122.6, 120.6, 47.9, 33.4, 26.5, 26.2; MS (ESI) calcd for C₁₈H₁₈N₂ [M+H]⁺: 263.15, found 263.04

2-(pentan-3-yl)-1,10-phenanthroline (12)
Following the general procedure II, 3-ethoxy-2,2-diethylcyclobutanone (38 mg, 0.22 mmol), 8-aminoquinoline (16 mg, 0.11 mmol), BF₃·OEt₂ (1.0 equiv, 0.11 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 12 (22 mg, yellow oil) was isolated in 79% yield. ¹H-NMR (400 MHz, CDCl₃) δ (ppm) 9.27 (dd, J = 1.76 Hz, J = 4.36 Hz, 1H), 8.24 (dd, J = 1.64 Hz, J = 8.04 Hz, 1H), 8.19 (d, J = 8.32 Hz, 1H), 7.78 (d, J = 8.72 Hz, 1H), 7.74 (d, J = 8.76 Hz, 1H), 7.61 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.53 (d, J = 8.32 Hz, J = 8.00 Hz, 1H), 7.50 (dd, J = 4.36 Hz, J = 8.04 Hz, 1H), 7.17 - 7.09 (m, 6H), 4.62 (s, 2H), 2.22 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 161.7, 150.3, 146.1, 145.7, 136.5, 136.0, 130.5, 128.8, 126.9, 126.4, 126.2, 125.7, 122.7, 122.3, 43.5, 19.9; MS (ESI) calcd for C₂₀H₁₆N₂ [M+H]⁺: 285.13, found 285.12
Hz, 1H), 3.30 - 3.23 (m, 1H), 1.94 - 1.81 (m, 4H), 0.90 (t, J = 7.40 Hz, 6H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 166.8, 150.4, 146.4, 145.7, 136.1, 136.0, 128.9, 127.2, 126.5, 125.5, 122.6, 121.0, 51.7, 28.2, 12.1; MS (ESI) calcd for C$_{17}$H$_{18}$N$_2$ [M+H]$^+$: 251.15, found 251.03

2-isopropyl-3-methyl-1,10-phenanthroline (13)

Following the general procedure II, 3-ethoxy-2,2,4-trimethylcyclobutanone (44 mg, 0.28 mmol), 8-aminoquinoline (20 mg, 0.14 mmol), BF$_3$ ·OEt$_2$ (1.0 equiv, 0.14 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 13 (16 mg, white solid) was isolated in 50% yield.$^1$H-NMR (300 MHz, CDCl$_3$) δ (ppm) 9.20 (d, J = 4.38 Hz, 1H), 8.19 (d, J = 8.01 Hz, 1H), 7.91 (s, 1H), 7.69 (s, 2H), 7.56 (dd, J = 4.41 Hz, J = 8.04 Hz, 1H), 3.59 - 3.54 (m, 1H), 2.59 (s, 3H), 1.55 (d, J = 6.84 Hz, 6H); $^{13}$C-NMR (75 MHz, CDCl$_3$) δ (ppm) 166.5, 150.4, 146.6, 144.1, 136.7, 131.0, 128.5, 127.4, 126.2, 33.3, 21.8, 19.3; MS (ESI) calcd for C$_{16}$H$_{16}$N$_2$ [M+H]$^+$: 237.13, found 237.07

3-ethyl-2-isopropyl-1,10-phenanthroline (14)

Following the general procedure II, 3-ethoxy-4-ethyl-2,2-dimethylcyclobutanone (71 mg, 0.42 mmol), 8-aminoquinoline (30 mg, 0.21 mmol), BF$_3$ ·OEt$_2$ (1.0 equiv, 0.21 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 14 (27 mg, white solid) was isolated in 52% yield.$^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.24 (dd, J = 1.76 Hz, J = 4.36 Hz, 1H), 8.22 (dd, J = 1.76 Hz, J = 8.04 Hz, 1H), 7.91 (s, 1H), 7.75 (d, d, J = 8.76 Hz, 1H), 7.70 (d, J = 8.72 Hz, 1H), 7.58 (dd, J = 4.36 Hz, J = 8.00 Hz, 1H), 3.65 - 3.58 (m, 1H), 2.97 (q, J = 7.44 Hz, 2H), 1.57 (d, J = 6.80 Hz, 6H), 1.40 (t, J = 7.48 Hz, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 166.2, 150.3, 146.5, 144.0, 136.6, 136.0, 134.7, 128.5, 127.5, 126.4, 125.5, 122.1, 32.3, 25.2, 22.5, 15.0; MS (ESI) calcd for C$_{16}$H$_{18}$N$_2$ [M+H]$^+$: 251.15, found 251.03

2-(4-chlorobenzyl)-1,10-phenanthroline (15)

Following the general procedure II, 2-(4-chloro-phenyl)-3-ethoxy-cyclobutanone (125 mg, 0.56 mmol), 8-aminoquinoline (40 mg, 0.28 mmol), BF$_3$ ·OEt$_2$ (1.0 equiv, 0.28 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 15 (27 mg, white solid) was isolated in 50% yield.$^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.20 (d, J = 7.40 Hz, 1H), 8.19 (d, J = 4.38 Hz, 1H), 7.91 (s, 1H), 7.69 (s, 2H), 7.56 (dd, J = 4.41 Hz, J = 8.04 Hz, 1H), 3.59 - 3.54 (m, 1H), 2.59 (s, 3H), 1.55 (d, J = 6.84 Hz, 6H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 166.8, 150.4, 146.4, 145.7, 136.1, 136.0, 128.9, 127.2, 126.5, 125.5, 122.6, 121.0, 51.7, 28.2, 12.1; MS (ESI) calcd for C$_{17}$H$_{18}$N$_2$ [M+H]$^+$: 251.15, found 251.03
molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 15 (54 mg, slight yellow oil) was isolated in 64% yield. $^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.26 (dd, $J = 1.76$ Hz, $J = 4.36$ Hz, 1H), 8.27 (dd, $J = 1.76$ Hz, $J = 8.08$ Hz, 1H), 8.13 (d, $J = 8.28$ Hz, 1H), 7.77 (s, 2H), 7.65 (dd, $J = 4.40$ Hz, $J = 8.08$ Hz, 1H), 7.35 (d, $J = 8.28$ Hz, 1H), 7.29 (s, 4H), 4.61 (s, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 161.4, 150.5, 146.1, 145.7, 138.0, 136.7, 136.1, 132.4, 130.9, 128.9, 128.8, 127.1, 126.4, 126.1, 123.0, 122.9, 45.0; MS (ESI) calcd for C$_{19}$H$_{13}$ClN$_2$ [M+H]$^+$: 305.08, found 305.04

**2-(naphthalen-1-ylmethyl)-1,10-phenanthroline (16)**

Following the general procedure II, 3-ethoxy-2-naphthalen-1-yl-cyclobutanone (133 mg, 0.56 mmol), 8-aminquinoline (40 mg, 0.28 mmol), BF$_3$·OEt$_2$ (1.0 equiv, 0.28 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 40 : 1). Finally, compound 16 (42 mg, slight yellow oil) was isolated in 47% yield. $^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.30 (dd, $J = 1.68$ Hz, $J = 4.36$ Hz, 1H), 8.27 (dd, $J = 1.72$ Hz, $J = 8.08$ Hz, 1H), 8.07 (d, $J = 8.44$ Hz,1H), 7.99 (d, $J = 8.32$ Hz, 1H), 7.88 (d, $J = 8.08$ Hz, 1H), 7.83 (dd, $J = 1.84$ Hz, $J = 7.20$ Hz, 1H), 7.76 (d, $J = 8.76$ Hz, 1H), 7.72 (d, $J = 8.76$ Hz, 1H), 7.66 (dd, $J = 4.36$ Hz, $J = 8.04$ Hz, 1H), 7.43-7.52 (m, 3H), 7.38-7.40 (m, 1H), 7.16 (d, $J = 8.32$ Hz, 1H), 5.12 (s, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 162.0, 150.5, 146.2, 145.8, 136.5, 136.1, 135.3, 134.1, 132.4, 128.9, 128.6, 127.6, 127.0, 126.5, 126.2, 125.8, 125.7, 125.7, 124.9, 122.9, 122.6, 43.4; MS (ESI) calcd for C$_{23}$H$_{16}$N$_2$ [M+H]$^+$: 321.13, found 321.11

**2-(naphthalen-2-ylmethyl)-1,10-phenanthroline (17)**

Following the general procedure II, 3-ethoxy-2-naphthalen-2-yl-cyclobutanone (133 mg, 0.56 mmol), 8-aminquinoline (40 mg, 0.28 mmol), BF$_3$·OEt$_2$ (1.0 equiv, 0.28 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (DCM : MeOH = 80 : 1). Finally, compound 17 (39 mg, slight yellow oil) was isolated in 44% yield. $^1$H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.26 (dd, $J = 1.68$ Hz, $J = 4.32$ Hz, 1H), 8.20 (dd, $J = 1.68$ Hz, $J = 8.08$ Hz, 1H), 8.03 (d, $J = 8.32$ Hz, 1H), 7.76-7.80 (m, 4H), 7.70 (d, $J = 1.44$ Hz, 2H), 7.60 (dd, $J = 4.36$ Hz, $J = 8.08$ Hz, 1H), 7.41-7.47 (m, 3H), 7.35 (d, $J = 8.28$ Hz, 1H), 4.80 (s, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ (ppm) 161.9, 150.4, 146.2, 145.7,
137.1, 136.5, 136.1, 133.7, 132.3, 128.9, 128.3, 128.0, 127.7, 127.6, 127.1, 126.5, 126.1, 125.9, 125.6, 123.3, 122.8, 45.9; MS (ESI) calcd for C_{13}H_{16}N_{2} [M+H]^+ : 321.13, found 321.07

8-azido-2-isopropyl-3-methylquinoline (20)
Following the general procedure, 1, 3-ethoxy-2,2,4-trimethylcyclobutanone (47 mg, 0.30 mmol), 2-azidoaniline (20 mg, 0.15 mmol) and BF₃·OEt₂ (1.0 equiv, 0.15 mmol) were used. The flask was coated with aluminum foil. The reaction mixture was stirred at room temperature under atmosphere of Argon for 12h. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 80 : 1). Finally, compound 20 (16 mg, colorless oil) was isolated in 48% yield. ³¹H-NMR (400 MHz, CDCl₃) δ (ppm) 7.83 (s, 1H), 7.44 - 7.39 (t, J = 1.28 Hz, 6H); 31C-NMR (100 MHz, CDCl₃) δ (ppm) 8.06 (d, J = 8.52 Hz, 1H), 7.53 (dd, J = 1.20 Hz, J = 8.12 Hz, 1H), 7.41 - 7.37 (m, 2H), 7.26 (dd, J = 1.28 Hz, J = 7.48 Hz, 1H), 3.48 - 3.39 (m, 1H), 2.20 - 2.15 (m, 2H), 1.99 - 1.88 (m, 4H), 1.77 - 1.74 (m, 2H); ³¹C-NMR (100 MHz, CDCl₃) δ (ppm) 165.5, 141.6, 136.4, 127.8, 125.5, 123.8, 121.5, 118.7, 48.6, 33.4, 26.0; MS (ESI) calcd for C_{13}H_{16}N_{2} [M+H–N₃]^+ : 211.12, found 211.06

8-azido-2-cyclopentylquinoline (21)
Following the general procedure, 1, 3-ethoxyspiro[3.4]octan-1-one (75 mg, 0.45 mmol), 2-azidoaniline (30 mg, 0.22 mmol) and BF₃·OEt₂ (1.0 equiv, 0.22 mmol) were used. The flask was coated with aluminum foil. Then, the reaction was stirred at 50°C overnight. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 80 : 1). Finally, compound 21 (38 mg, colorless oil) was isolated in 72% yield. ³¹H-NMR (400 MHz, CDCl₃) δ (ppm) 8.06 (d, J = 8.52 Hz, 1H), 7.53 (dd, J = 1.20 Hz, J = 8.12 Hz, 1H), 7.41 - 7.37 (m, 2H), 7.26 (dd, J = 1.28 Hz, J = 7.48 Hz, 1H), 3.48 - 3.39 (m, 1H), 2.20 - 2.15 (m, 2H), 1.99 - 1.88 (m, 4H), 1.77 - 1.74 (m, 2H); ³¹C-NMR (100 MHz, CDCl₃) δ (ppm) 165.5, 141.6, 136.4, 127.8, 125.5, 123.8, 121.5, 118.7, 48.6, 33.4, 26.0; MS (ESI) calcd for C_{13}H_{16}N [M+H-N₂]^+ : 211.12, found 211.06

2-isopropyl-3-methylquinolin-8-amine (23)
Following the general procedure, 1, 8-azido-2-isopropyl-3-methylquinoline (18 mg, 0.08 mmol) were added to a solution of triphenylphosphine (25 mg, 0.10 mmol) in anhydrous methanol. The flask was coated with aluminum foil. Then, the reaction was stirred at 50°C overnight. After completion of the reaction, the residue was purified by silical gel column chromatography.
(Petroleum ether : EtOAc = 40 : 1), Finally, compound 23 (14 mg, colorless oil) was isolated in 88% yield.\textsuperscript{1} H-NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 7.74 (s, 1H), 7.22 (t, \(J = 7.84\) Hz, 1H), 7.04 (dd, \(J = 0.88\) Hz, \(J = 8.12\) Hz, 1H), 6.84 (dd, \(J = 0.96\) Hz, \(J = 7.40\) Hz, 1H), 4.97 (brs, 2H), 3.41 - 3.34 (m, 1H), 2.48 (s, 3H), 1.36 (d, \(J = 6.72\) Hz, 6H); \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 163.4, 143.5, 136.6, 135.8, 129.1, 127.5, 126.3, 115.1, 109.0, 32.0, 21.9, 19.0; MS (ESI) calcd for C\textsubscript{13}H\textsubscript{16}N\textsubscript{2}[M+H]\textsuperscript{+}: 201.13, found 201.05

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\text{N} \\
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**2-cyclopentylquinolin-8-amine (24)**

Following the general procedure I, 8-azido-2-cyclopentylquinoline (33 mg, 0.14 mmol) were added to a solution of triphenylphosphine (44 mg, 0.17 mmol) in anhydrous methanol. The flask was coated with aluminum foil. Then, the reaction was stirred at 50\degree C overnight. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 40 : 1), Finally, compound 24 (28 mg, colorless oil) was isolated in 95% yield.\textsuperscript{1} H-NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 7.98 (d, \(J = 8.48\) Hz, 1H), 7.32 - 7.26 (m, 2H), 7.13 (dd, \(J = 1.08\) Hz, \(J = 8.08\) Hz, 1H), 6.93 (dd, \(J = 1.16\) Hz, \(J = 7.44\) Hz, 1H), 5.00 (brs, 2H), 3.41 - 3.35 (m, 1H), 2.20 – 2.13 (m, 2H), 2.01 - 1.85 (m, 4H), 1.79 - 7.74 (m, 2H); \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 163.2, 143.6, 137.6, 136.0, 127.2, 126.2, 121.0, 115.9, 110.0, 48.3, 33.4, 26.0; MS (ESI) calcd for C\textsubscript{14}H\textsubscript{16}N\textsubscript{2}[M+H]\textsuperscript{+}: 213.13, found 213.09

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\text{N} \\
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**2,9-diisopropyl-1,10-phenanthroline (25)**

Following the general procedure II, 3-ethoxy-2,2-dimethylcyclobutanone (28 mg, 0.20 mmol), 2-isopropyl-8-aminoquinoline (18 mg, 0.10 mmol), BF\textsubscript{3}·OEt\textsubscript{2} (1.0 equiv, 0.10 mmol) and crushed 4 Å molecular sieves (150\% wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48h. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 2 : 1). Finally, compound 25 (16 mg, colorless oil) was isolated in 62% yield.\textsuperscript{1} H-NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 8.16 (d, \(J = 8.32\) Hz, 2H), 7.70 (s, 2H), 7.56 (d, \(J = 8.32\) Hz, 2H), 3.61 - 3.54 (m, 2H), 1.79 - 7.74 (m, 2H); \textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) (ppm) 163.2, 143.6, 137.6, 136.0, 127.2, 126.2, 121.0, 115.9, 110.0, 48.3, 33.4, 26.0; MS (ESI) calcd for C\textsubscript{18}H\textsubscript{20}N\textsubscript{2}[M+H]\textsuperscript{+}: 265.16, found 265.07
2,9-diisopropyl-3,8-dimethyl-1,10-phenanthroline (26)
Following the general procedure II, 3-ethoxy-2,2,4-trimethylcyclobutanone (28 mg, 0.18 mmol), 2-isopropyl-3-methyl-8-aminoquinoline (18 mg, 0.09 mmol), BF₃·OEt₂ (1.0 equiv, 0.09 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48 h. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 20 : 1). Finally, compound 26 (14 mg, white solid) was isolated in 53% yield.¹H-NMR (400 MHz, CDCl₃) δ (ppm) 7.85 (s, 2H), 7.59 (s, 2H), 3.53 – 3.46 (m, 2H), 2.55 (s, 6H), 1.53 (d, J = 6.72 Hz, 12H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 165.5, 144.0, 136.1, 129.8, 127.0, 124.9, 32.8, 21.7, 19.0; MS (ESI) calcd for C₁₈H₂₀N₂ [M+H]+: 265.16, found 265.07

2,9-dicyclopentyl-1,10-phenanthroline (27)
Following the general procedure II, 3-ethoxy-spiro[3.4]octan-1-one (40 mg, 0.24 mmol), 2-cyclopentyl-8-aminoquinoline (25 mg, 0.12 mmol), BF₃·OEt₂ (1.0 equiv, 0.12 mmol) and crushed 4 Å molecular sieves (150%wt) were used. The reaction mixture was stirred at room temperature under atmosphere of Argon for 48 h. After completion of the reaction, the residue was purified by silical gel column chromatography (Petroleum ether : EtOAc = 10 : 1). Finally, compound 27 (25 mg, white solid) was isolated in 68% yield.¹H-NMR (400 MHz, CDCl₃) δ (ppm) 8.21 (d, J = 8.36 Hz, 2H), 7.74 (s, 2H), 7.60 (d, J = 8.40 Hz, 2H), 3.80 - 3.76 (m, 2H), 2.40 - 2.33 (m, 4H), 2.01 - 1.92 (m, 8H), 1.91 - 1.81 (m, 4H); ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 167.0, 136.8, 127.3, 125.5, 121.4, 48.6, 34.2, 26.2; MS (ESI) calcd for C₂₂H₂₆N₂ [M+H]+: 317.19, found 317.12