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Supporting Information

Interplay of Interactions Governing the Dynamic Conversions of Acyclic and Macrocyclic Helicates

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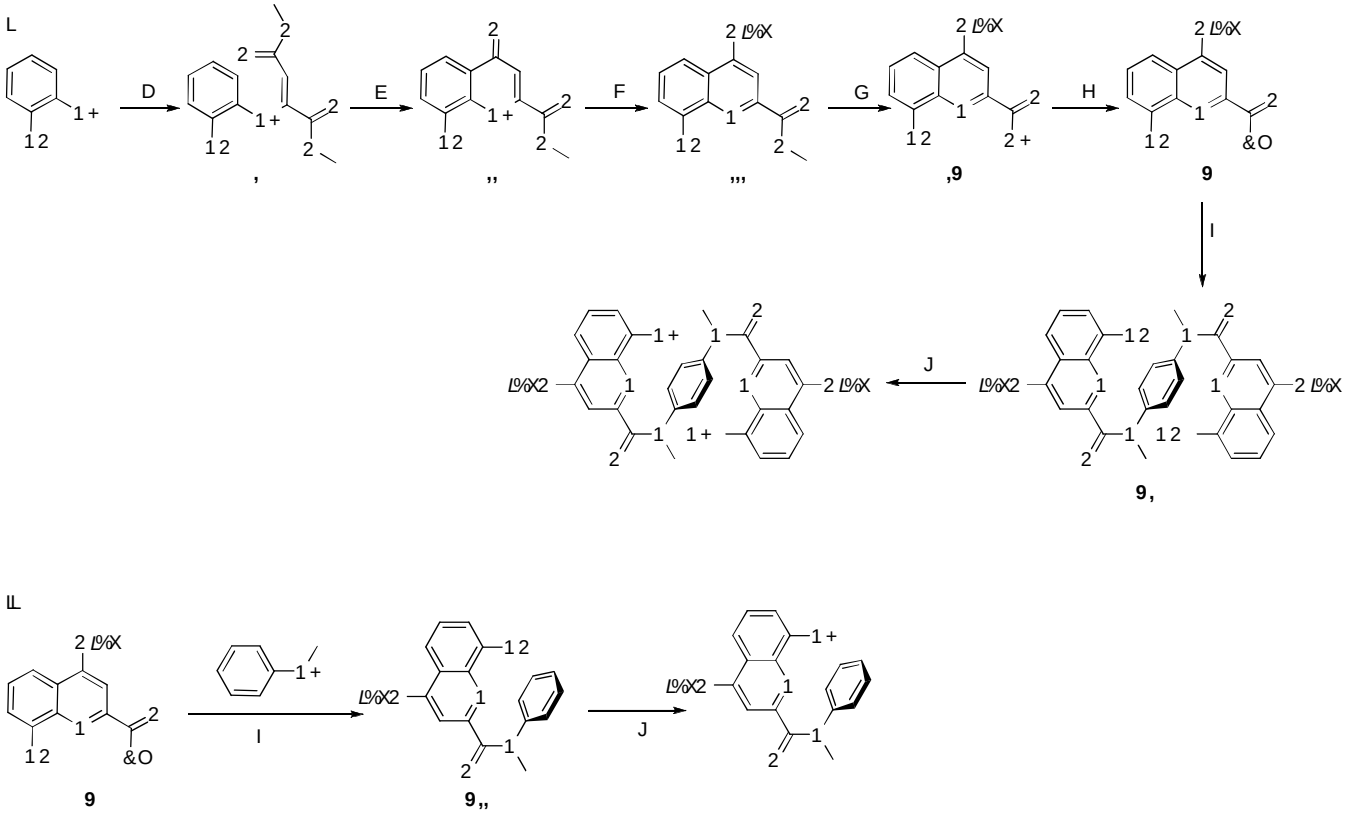
Experimental

General. All reactions were carried out in dry glassware with an Argon overpressure. Unless otherwise noted, all reagents were purchased from Aldrich or Acros and used without further purification. THF and CH_2Cl_2 were dried by passage through anhydrous alumina columns whereas diisopropylethylamine (DIEA) was distilled from CaH_2. Compound **V**, 4-isobutoxy-8-nitroquinoline-2-carbonyl chloride was prepared following a slightly modified (as described below) version of our previously-described procedure;[1] N1,N4-dimethylbenzene-1,4-diamine[2] and 1,10-phenanthroline-2,9-dicarbaldehyde[3] were prepared according to the literature. NMR spectra were recorded on Bruker Aspect 300, Bruker DRX-400, Bruker Avance 500 Cryo, and Bruker 500 TCI-ATM Cryo Spectrometers. Chemical shifts are reported in ppm and are referenced to the solvent signals of $CDCl_3$ (δ = 7.26 ppm for ^1H, 77.2 ppm for ^{13}C). All coupling constants are reported in Hz. High-resolution electrospray ionization time of flight (HR-ESI) mass spectra were obtained in positive ion mode. Silica gel chromatography was performed by using Merck Kieselgel Si 60.



Scheme S1. a) DMAD, MeOH, 12h reflux; b) PPA, 130°C, 3h; c) isobutanol, DIAD, PPh_3, THF, RT overnight; d) KOH, MeOH/THF, RT 12h; e) $SOCl_2$, 20 min reflux; f) CH_2Cl_2, DIEA, 12h RT; g) Pd/C, Ammonium formate, Ammonium metavanadate, H_2, EtOAc/MeOH/H_2O, RT 4h

Synthesis of I: To a solution of 2-nitroaniline (13.8 g, 100 mmol) in 150 mL methanol an equimolar amount of dimethylbut-2-ynedioate (100 mmol, 14.2 g, 12.25 mL) was added. The resulting mixture was stirred at reflux for 24 hours. The reaction mixture was then cooled to -18°C for precipitation. The resulting yellow prisms were collected by filtration, washed with cold methanol and dried under reduced pressure to yield 20.6 g (74%) of dimethyl-2-(2-nitrophenylamino)maleate **I**. ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 11.11 (1H, bs, NH), δ = 8.14 (1H, dd, *J* = 1.4, 8.3 Hz), δ = 7.46 (1H, t, *J* = 8.8 Hz), δ = 7.08 (1H, t, *J* = 8.4 Hz), δ = 6.78 (1H, dd, *J* = 1.3, 8.4 Hz), δ = 5.04 (1H, s), δ = 3.81 (3H, s), δ = 3.76 (3H, s).

Synthesis of II: A mixture of 2-(2-nitrophenylamino)maleate **I** (17.8 g, 63 mmol) and polyphosphoric acid (90 g) was placed in a 500 mL round bottom flask equipped with a rotor and a mechanical stirrer. The reaction was vigorously stirred at 130°C for 3 hours. The resulting slurry was poured into saturated $NaHCO_3$ at 0°C. The precipitate was subsequently filtered and washed with distilled water. The product was purified by precipitation from cold methanol to yield 9.5 g (61%) of methyl 1,4-dihydro-8-nitro-4-oxoquinoline-2-carboxylate **II**. ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 11.80 (1H, bs), δ = 8.74 (2H, m), δ = 7.47 (1H, t, *J* = 8.8 Hz), δ = 7.08 (1H, s), δ = 4.09 (3H, s).

Synthesis of III: Under an inert atmosphere, methyl-1,4-dihydro-8-nitro-4-oxoquinoline-2-carboxylate **II** (20.48 mmol, 5.08 g), 2-methylpropanol (1.1 eq, 22.5 mmol, 2.08 mL) and triphenylphosphine (1.05 eq, 21.5 mmol, 5.64 g) were suspended in 45 mL anhydrous THF. Diisopropyl azodicarboxylate (1.1 eq) was then added to this mixture at 0°C resulting in complete dissolution of the precipitate. The mixture was stirred for 4 hours at room temperature. The product was purified by crystallization from MeOH/CH_2Cl_2 (slow evaporation). Crystals were collected by filtration, washed with cold methanol and dried under reduced pressure to yield 4.87 g of a yellow solid (78%). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.48 (1H, dd, *J* = 1.3, 6.7 Hz), δ = 8.11 (1H, dd, *J* = 1.3, 6.0 Hz), δ = 7.67 (2H, m), δ = 4.09 (2H, d, *J* = 6.2 Hz), δ = 4.02 (3H, s), δ = 2.25 (1H, m), δ = 1.14 (6H, d, *J* = 6.7 Hz)

Synthesis of IV: Methyl 4-isobutoxy-8-nitroquinoline-2-carboxylate **III** (16.0 mmol, 4.85 g) and 200 mL of THF/MeOH (2/1) were introduced into a 500 mL round bottomed flask equipped with a large magnetic stirrer. KOH (2.5 eq, 40 mmol, 2.24 g) was then added to

this mixture. The resulting slurry was stirred overnight at ambient temperature. The reaction mixture was then quenched by addition of 100 mL of 5% aqueous citric acid and diluted with 100 mL CH_2Cl_2. The layers were separated and the organic layer was washed with distilled water and saturated NaCl (aq). The combined organic layers were dried over $MgSO_4$ and filtered. After rotary evaporation 4.6 g of 4-isobutoxy-8-nitroquinoline-2-carboxylic acid **IV** was isolated as a yellow solid (quantitative). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.56 (1H, dd, *J* = 81.3, 6.2 Hz), δ = 8.22 (1H, dd, *J* = 1.3 Hz, 6.5 Hz), δ = 7.74 (2H, m), δ = 4.15 (2H, d, *J* = 6.2 Hz), 2.33 (1H, m), δ = 1.16 (6H, d, *J* = 6.2 Hz).

Synthesis of V: 4-isobutoxy-8-nitroquinoline-2-carboxylic acid (4.6 g, 16.0 mmol) and $SOCl_2$ 80 mL were introduced into a round bottomed flask equipped with a magnetic stirring bar and a reflux condenser. The round bottomed flask was placed in an oil bath previously heated to 90°C. The reaction mixture was stirred at 90°C for 20 min and subsequently diluted with 80 mL toluene. The solvents were removed by azeotropic distillation on a rotary evaporator and the residue was then thoroughly dried under reduced pressure to yield 4.9 g of 4-isobutoxy-8-nitroquinoline-2-carbonyl **V** chloride as a yellowish solid (quantitative). The product was used without further purification. ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.56 (1H, dd, *J* = 1.3, 6.2 Hz), δ = 8.18 (1H, dd, *J* = 1.3, 6.5 Hz), δ = 7.74 (1H, t, *J* = 8.3 Hz), δ = 7.53 (1H, s), δ = 4.18 (2H, d, *J* = 7.2 Hz), δ = 2.33 (1H, m), δ = 1.13 (6H, d, *J* = 6.3 Hz).

Synthesis of VI: N1,N4-dimethylbenzene-1,4-diamine (136 mg, 1.00 mmol) and N,N-Diisopropylethylamine (5.0 mmol, 0.83 mL) were dissolved in freshly distilled dichloromethane (10 mL) under an inert gas atmosphere. The flask was then cooled to 0°C using an ice bath. In a separate flask, 4-isobutoxy-8-nitroquinoline-2-carbonyl chloride **V** (2.1 eq, 2.1 mmol) was dissolved in dry CH_2Cl_2 (10 mL). A solution of 4-isobutoxy-8-nitroquinoline-2-carbonyl chloride was then added via stainless steel cannula to the solution of N1,N4-dimethylbenzene-1,4-diamine. The mixture was stirred at ambient temperature overnight. After evaporation of the solvent, the product was purified by crystallisation from MeOH/$CHCl_3$. The yellow prisms of N,N'-(1,4-phenylene)bis(4-isobutoxy-N-methyl-8-nitroquinoline-2-carboxamide) **VI** were collected by filtration and washed several times with cold methanol (585 mg, 86 %). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.32 (2H, bs), δ = 7.71 (2H, bs), δ = 7.47 (2H, bs), δ = 7.37 (2H, s), one aromatic signal is obscured by solvent signal, δ = 6.96 (4H, m), δ = 4.08 (4H, d, *J* = 6.1 Hz), δ = 3.48 (6H, s), δ = 2.28 (1H, m), δ = 1.15 (12H, d, *J* = 6.2 Hz). ^{13}C NMR (300 MHz,

300K, $CDCl_3$): δ = 167.28, 162.19, 156.36, 147.93, 142.80, 127.39, 125.66, 124.88, 123.54, 122.12, 102.56, 75.41, 38.72, 28.09, 19.18. ESI-HRMS: *m/z:* 681.3448 ($[M+H]^+$) (calcd for $C_{36}H_{36}N_6O_8$ *m/z* 680,2642).

Synthesis of 1: In a round-bottomed flask, N,N'-(1,4-phenylene)bis(4-isobutoxy-N-methyl-8-nitroquinoline-2-carboxamide) **VI** (400 mg; 0.58 mmol) was suspended in an ethyl acetate / methanol mixture (9/1) (100 mL). Catalytic amounts of Pd / C (20 w%) and ammonium metavanadate (20 w%) were added to the suspension, followed by ammonium formate (2 g). The mixture was stirred at reflux overnight. The reaction mixture was then filtered through Celite which was rinsed with CH_2Cl_2. The organic layer was subsequently washed with saturated NaCl (aq) and dried over $MgSO_4$. After filtration and rotary evaporation a greenish solid was obtained (356 mg, quantitative). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 7.54 (2H, bs), some aromatic signals are obscured by solvent signal, δ = 7.18 (2H, s), δ = 6.93 (2H, bs), δ = 4.01 (4H, d, J = 5.9 Hz), δ = 3.53 (6H, s), δ = 2.25 (2H, m), δ = 1.13 (12H, d, J = 6.2 Hz). ^{13}C NMR (75 MHz, 300K, $CDCl_3$): δ = 166.78, 161.69, 155.86, 147.44, 142.29, 137.94, 126.89, 125.15, 124.37, 123.03, 121.62, 102.06, 74.91, 38.21, 38.16, 27.59, 18.68. ESI-HRMS: m/z: 621.3180 ($[M+H]^+$) (calcd for $C_{36}H_{40}N_6O_4$ m/z 620,3111).

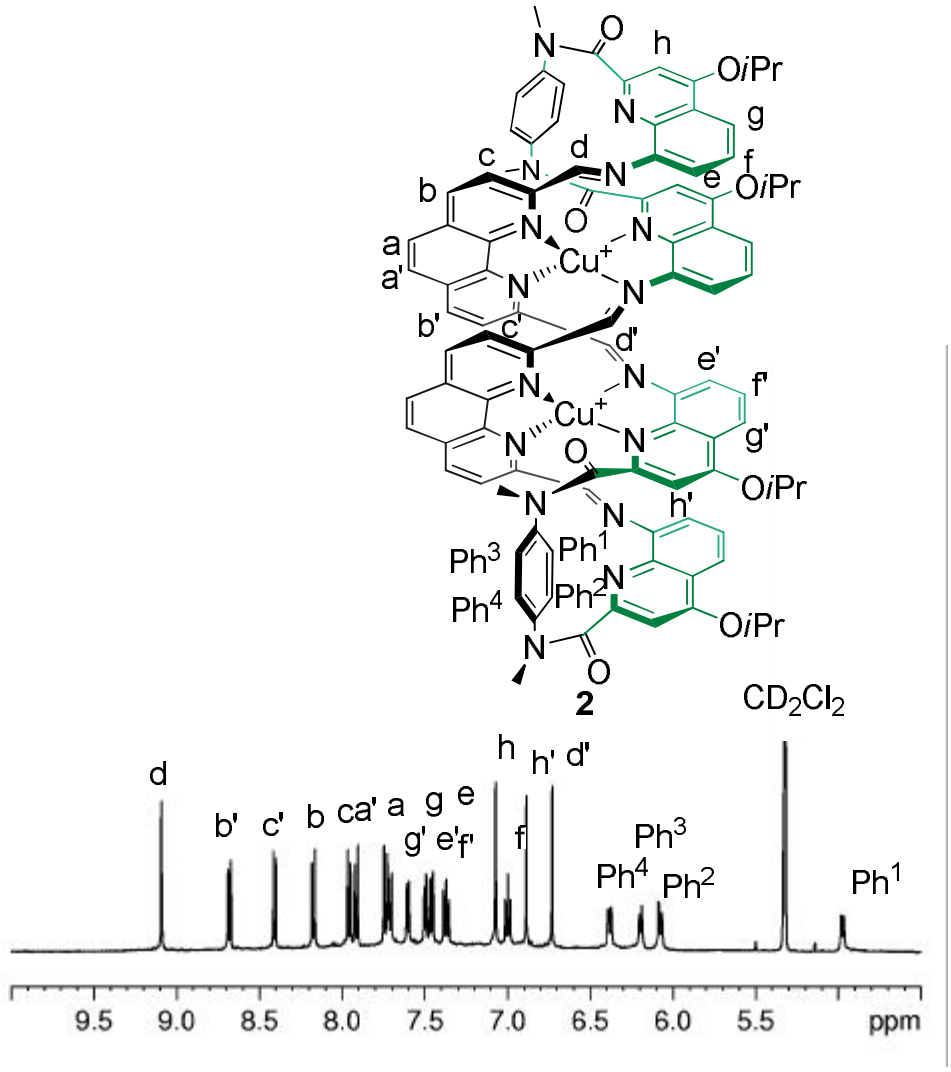


Figure S1. ^{1}H NMR assignment of macrocycle **2**.

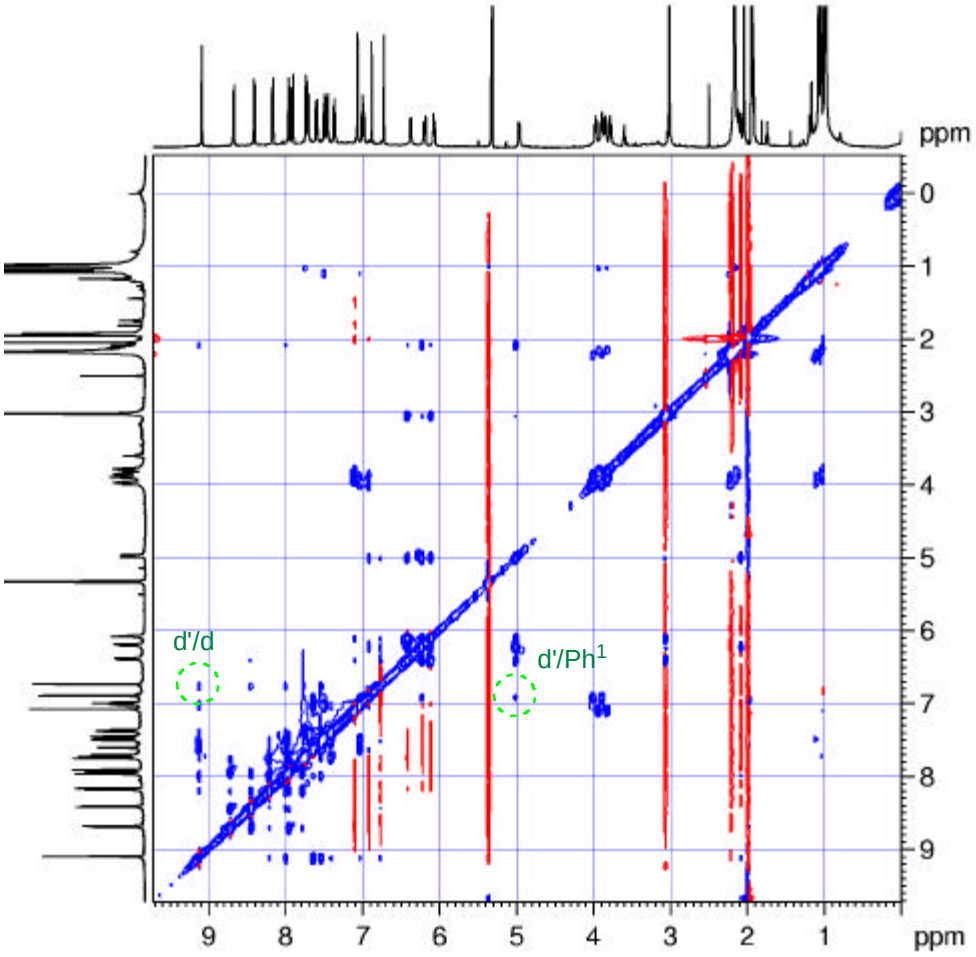


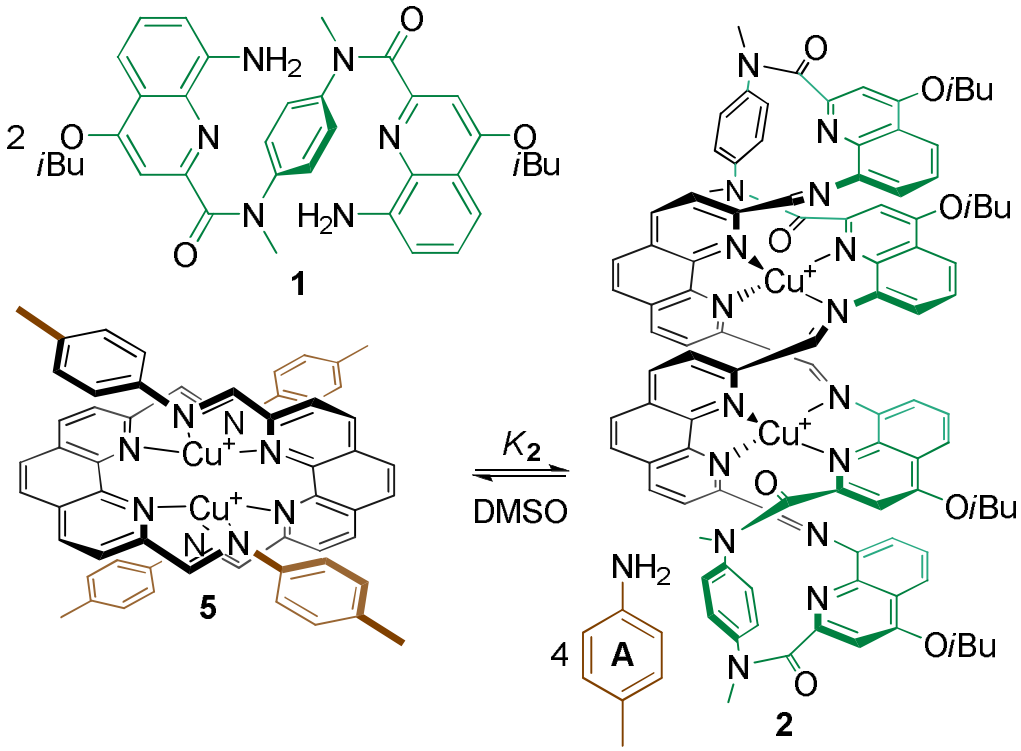
Figure S2. ^{1}H NOESY spectrum of macrocycle **2**.

Synthesis of VII: N-methylaniline (1.1 mmol, 120 mL) and N,N-Diisopropylethylamine (5 mmol, 0.83 mL) were dissolved in 10 mL of dry CH_2Cl_2 and placed under an inert gas atmosphere. In a separate flask, 4-isobutoxy-8-nitroquinoline-2-carbonyl chloride **V** (1.0 mmol) was dissolved in dry CH_2Cl_2 (10 mL). Solution of 4-isobutoxy-8-nitroquinoline-2-carbonyl chloride was then added via a stainless steel cannula to the solution of N-methylaniline. Mixture was stirred at ambient temperature overnight. After evaporation of the solvents, residue was purified on silica gel (CH_2Cl_2/MeOH : 99.5/0.5) to yield an orange solid (86 %). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$): δ = 8.34 (1H, d, *J* = 7.7 Hz), δ = 7.82 (1H, d, *J* = 7.4 Hz), δ = 7.50 (1H, t, *J* = 7.1 Hz), δ = 7.41-7.12 (6H,ms), δ = 4.01 (2H, d, *J* = 6.2 Hz), δ = 3.55 (3H, s), δ = 2.27 (1H, m), δ = 1.13 (6H, d, *J* = 6.2 Hz). ^{13}C NMR (75 MHz, 300K, $CDCl_3$): δ = 167.70, 162.14, 156.69, 148.09, 144.33, 138.69, 129.15, 129.01, 126.95, 126.75, 125.73, 124.87, 123.92, 122.10, 102.38, 102.27, 75.39, 28.08, 19.18. ESI-HRMS: *m/z:* 380.2781 ($[M+H]^+$) (calcd for $C_{21}H_{21}N_3O_4$ *m/z* 379,1532).

Synthesis of 3: Into a round bottomed flask, 4-isobutoxy-N-methyl-8-nitro-N-phenylquinoline-2-carboxamide **VII** (310 mg; 0.82 mmol) was suspended in 100 mL of EtOAc/MeOH mixture (9/1). Catalytic amounts of Pd / C (20 w) and of ammonium metavanadate (10 w%) along with 2 g of ammonium formate were added to the mixture. The suspension was stirred at reflux overnight. The reaction mixture was then filtered through Celite and solvents were removed by rotary evaporation to yield a dark green solid. The product was purified by precipitation from cold methanol (223 mg, 78 %). ^{1}H NMR (300 MHz, 300 K, $CDCl_3$) : δ = 7.42 (1H, d, *J* = 7.6 Hz), several signal are obscured by the solvent signal δ = 7.16 (2H,m), 6.74 (1H, d, *J* = 7.7 Hz), δ = 3.95 (2H, d, *J* = 5.4 Hz), δ = 3.57 (3H, s), δ = 2.22 (1H, m), δ = 1.10 (6H, d, *J* = 6.0 Hz). ^{13}C NMR (75 MHz, 300K, $CDCl_3$): δ = 167.55, 161.69, 149.90, 143.68, 136.61, 128.47, 126.99, 125.95, 125.83, 121.19, 110.07, 109.06, 100.69, 74.26, 38.61, 29.22, 27.66, 18.76. ESI-HRMS: *m/z:* 350.5957 ($[M+H]^+$) (calcd for $C_{21}H_{23}N_3O_2$ *m/z* 349.1790).

Determination of Equilibrium Constant

One may assign equilibrium constant K_2 to the expression given in Scheme S2.



Scheme S2.

Since $[\mathbf{2}]_0 = [\mathbf{A}]_0 = 0$, $[\mathbf{1}]_0 = 2[\mathbf{5}]_0$, and (**5**, **2**, **1**, and **A**) were the only four species experimentally observed, one may state that [**1**] = 2[**5**] and 4[**2**] = [**A**]. The equilibrium constant K_2 for this reaction may thus be expressed:

$$K_2 = \frac{[\mathbf{2}][\mathbf{A}]^4}{[\mathbf{5}][\mathbf{1}]^2} = \frac{[\mathbf{2}](4[\mathbf{2}])^4}{[\mathbf{5}](2[\mathbf{5}])^2} = \frac{64[\mathbf{2}]^5}{[\mathbf{5}]^3} \qquad (\mathbf{S1})$$

The concentrations of **5** and **2** were determined by ^{1}H NMR integration (measured against tetramethylsilane at constant concentration) allowing determination of the equilibrium constants noted in Table S1.

Table S1

Temperature (K)	[**2**] (10^{-3} mol L^{-1})	[**5**] (10^{-3} mol L^{-1})	ln(K_2)
373	5.4	1.68	-2.78
383	5.6	1.48	-2.22
393	5.86	1.22	-1.41
403	6.01	1.07	-0.89

Van ‘t Hoff analysis of this equilibrium thus allowed for the entropy and enthalpy of the reaction to be extracted through a linear least-squares fit of ln(K_2) plotted against T^{-1}.

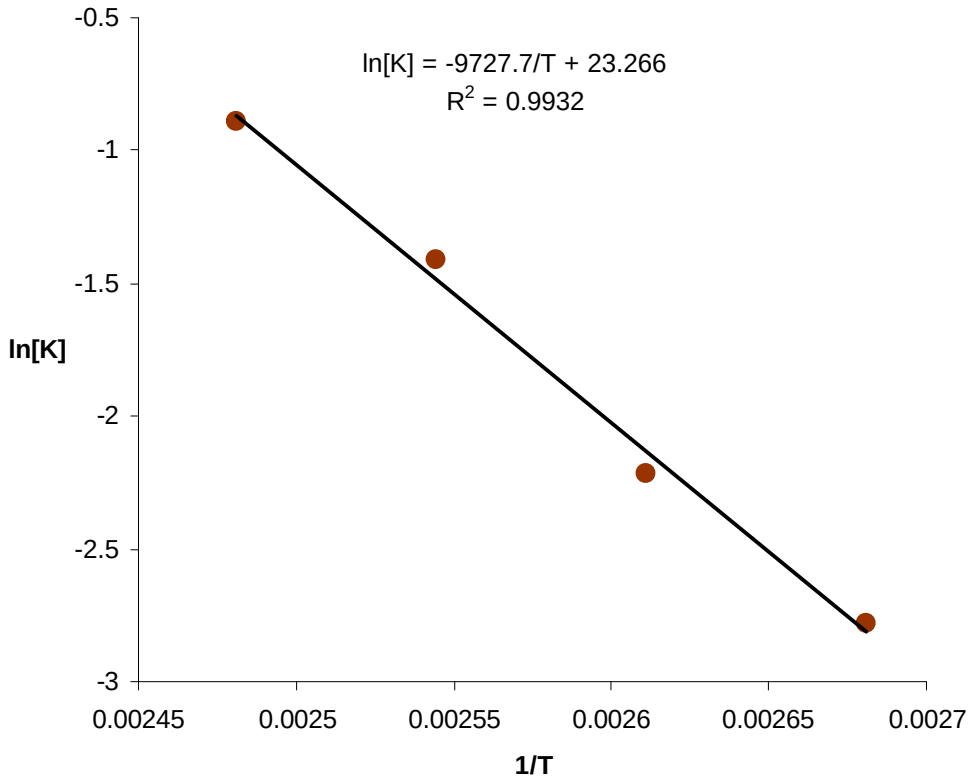


Figure S3. Van 't Hoff plot of the temperature-dependent equilibrium of Scheme S3.

The enthalpy of the reaction was given by the slope of the linear-least-squares fit ($-\Delta H°/(RT) = -9727.7$; $\Delta H° = 81$ kJ mol^{-1}), and from the intercept the entropy was obtained ($\Delta S°/R = 23.26$; $\Delta S° = 0.193$ kJ mol^{-1}K^{-1}).

References

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