Table 1. Thermodynamic data extracted from Figures 14-19 for the equilibrium of **13** and **16** over a range of temperatures.

8 (N)	[THF] (M)	ΔH (kcal/mol)	ΔS (cal/mol·K)
0.016	9.5	1.8 ± 0.1	-12.0 ± 0.7
0.018	10.5	1.70 ± 0.07	-12.4 ± 0.5
0.009	7.15	1.75 ± 0.05	-12.4 ± 0.5
0.0048	2.86	1.7 ± 0.1	-10.8 ± 0.5
0.005	11.3	1.89 ± 0.05	-11.7 ± 0.2
0.0489	7.5	2.01 ± 0.05	-10.2 ± 0.2
	Average:	1.8 ± 0.1	-11.6 ± 0.9

Table 2. Comparison of the rates of the 1,2-addition of PhCCLi (0.05 N) to mixed dimer **13** and **11** at -25 °C in THF/pentane solutions. Rate constants were acquired using ^{19}F NMR spectroscopy.

Substrate	[THF] (M)	$k_{obsd} \times 10^4$
11	4.61	35.7 ± 0.3
11	11.99	112 ± 2
13	4.61	0.160 ± 0.004
13	11.99	0.112 ± 0.004

Table 3. Data from Figure 21 fit to $[13] = \{(\alpha-1)k_{obsd}t + [13]_0^{-(1-\alpha)}\}^{-1/(\alpha-1)}$ to determine the order of the decay. The adjustable parameter α corresponds to the reaction order in **13**.

[PhCCLi] (N)	$\alpha 1$	$\alpha 2$
0.035	1.08 ± 0.01	1.09 ± 0.04
0.070	1.09 ± 0.02	1.08 ± 0.02
0.120	1.09 ± 0.02	1.03 ± 0.02
0.195	1.06 ± 0.02	1.05 ± 0.02
0.295	1.07 ± 0.01	1.03 ± 0.03
0.395	1.05 ± 0.02	1.01 ± 0.02
0.495	1.02 ± 0.02	1.06 ± 0.01
0.595	1.02 ± 0.02	0.99 ± 0.02
0.695	1.01 ± 0.02	1.04 ± 0.01

Average α: 1.05 ± 0.03

Table 4. Data from Figure 30 fit to $[11] = \{(\alpha-1)k_{obsd}t + [11]_0^{-(1-\alpha)}\}^{-1/(\alpha-1)}$ to determine the order of the decay. The adjustable parameter α corresponds to the reaction order in **11**.

[PhCCLi] (N)	$\alpha 1$	$\alpha 2$	$\alpha 3$
0.025	1.07 ± 0.02	1.07 ± 0.03	
0.050	1.02 ± 0.01	1.01 ± 0.01	
0.100	1.30 ± 0.05	0.99 ± 0.02	0.86 ± 0.04
0.150	0.97 ± 0.02	1.06 ± 0.07	
0.200	0.97 ± 0.02	0.90 ± 0.03	1.06 ± 0.03
0.250	1.00 ± 0.04	1.07 ± 0.02	
0.300	1.04 ± 0.03	1.00 ± 0.03	
0.400	0.93 ± 0.03	0.93 ± 0.06	

Average α: 1.01 ± 0.09

Rate Studies by In Situ IR Spectroscopy.

A typical rate constant was determined as follows. IR spectra were recorded using an in situ IR spectrometer fitted with a 30-bounce silicon-tipped probe. The IR probe was inserted through a nylon adapter and FETFE O-ring seal into an oven-dried cylindrical flask fitted with a magnetic stir bar and T-joint. The T-joint was fitted with a nitrogen line and septum for injections. The flask was heated under full-vacuum and flushed twice with nitrogen. Three separate stock solutions were prepared as follows. A PhCCLi solution was prepared by dissolving LiHMDS (3.073 g, 18.4 mmol) with 12.6 mL THF and 12.6 mL of pentane followed by the addition of phenylacetylene (1.68 mL, 15.3 mmol). A LiHMDS solution was prepared by dissolving LiHMDS (0.598 g, 3.6 mmol) in 17.5 mL of THF and 17.5 mL of pentane. The flask was charged with 5.9 mL of the PhCCLi solution and 3.9 mL of the LiHMDS solution. The new solution was cooled to 10 °C in a thermostatted bath for 20 minutes. A background spectrum was recorded, followed by addition of 0.2 mL of a 0.25 N solution of **8** while stirring. The solution of **8** was prepared by adding **5** (0.062 g, 0.25 mmol) and LiHMDS (0.063g, 0.38 mmol) in 0.875 mL of THF. Spectra were recorded every 30 seconds for 3 to 5 half-lives.

Rate Studies by ^{19}F NMR Spectroscopy.

I. 1,2-Addition of PhCCLi to mixed dimer **13**.

All tubes were prepared and stored at -78 °C prior to analysis. NMR tubes were prepared using stock solutions and sealed under partial vacuum. The tubes used for determination of PhCCLi order were prepared over a range of PhCCLi concentrations (0.04 N* to 0.70 N) so that all solutions were 0.005 N in subunit **8**, and 7.75 M in THF with a 0.10 N excess of LiHMDS. Tubes used to determine the solvent order were prepared over a range of THF concentrations (2.7 M to 11.3 M) so that all solutions were 0.005 N in subunit **8**, and 0.20 N in PhCCLi , and 0.10 N excess LiHMDS. An example of a typical tube preparation is as follows: After flame drying under high vacuum, the NMR tube equipped with a septum was flushed with argon and secured in a dry ice/acetone bath (-78 °C). The tube was then charged with 0.395 mL of a

0.76 N PhCCLi solution, 0.155 mL of a 0.109 N LiHMDS solution, and 0.050 mL of a 0.06 N solution of **8**. The sample was sealed under partial vacuum and stored at -78 °C. The NMR probe was cooled at 10 °C for over 30 minutes to assure temperature equilibration. The temperature was determined by chemical-shift difference of the two proton resonances of a sample of neat MeOH. The 90° pulse and T_1 of the ^{19}F resonance were determined with a 0.005 N solution of **8** in 10.2 M THF/pentane. The sample was quickly transferred from the -78 °C bath into the spectrometer, and was shimmed off the fluorine or proton spectrum. The experiment was set up to acquire 4 scans (acquisition time = 1.28 s, delay = 3.5 s) every 60 seconds, and data was collected for 4 to 5 half-lives. (The acquisition time plus delay was set to > 5 T_1s.) ^{19}F resonances were integrated relative to the fifth spectrum acquired (> 5 minutes into reaction to assure temperature equilibration). Rate constants were determined by fitting the integrations to a first-order decay (integration = integration$_0$e$^{-k_{obsd}t}$ + c).

* Pseudo-first order conditions were not necessary because PhCCLi is not consumed in the reaction, see Figure 3.

II. 1,2-Addition of PhCCLi to **11**.

All tubes were prepared and stored in a liquid nitrogen bath prior to analysis. Tubes were prepared using stock solutions and sealed under partial vacuum. The tubes used to determine the PhCCLi order were prepared over a range of PhCCLi concentrations (0.025 N* to 0.30 M) so that all solutions were 0.005 M in **11** and 8.64 M in THF. Tubes used to determine the solvent order were prepared over a range of THF concentrations (4.6 M to 12.0 M) so that all solutions were 0.005 M in **11**, and 0.05 N in PhCCLi, and 0.10 M excess of LiHMDS. An example of a typical tube preparation is as follows: after flame drying under high vac, the tube equipped with a septum was flushed with helium and secured in a liquid nitrogen bath. The tube was then charged with: 0.160 mL of a 0.75 N PhCCLi solution, 0.200 mL of neat THF, 0.120 mL of pentane, and 0.120 mL of a 0.025 M solution of **11**. The resulting frozen solution was sealed under partial vacuum and stored in a liquid nitrogen bath. The NMR probe was cooled (at -55 °C for PhCCLi order determination or -40 °C for THF order determination) for over 60 minutes to assure temperature

equilibration. The temperature was determined by chemical-shift difference of the two proton resonances of a sample of neat MeOH. The 90° pulse and T_1 of the ^{19}F resonance were determined with a 0.005 M solution of **11** in 6.1 M THF/pentane. The tube was transferred from the liquid nitrogen bath to a -78 °C bath to thaw the solution, then quickly transferred into the spectrometer, and shimmed off the fluorine or proton spectrum. The experiment was set up to take 2 scans (acquisition time = 0.640 s, delay = 3.5 s) every 20 seconds, and data was collected for 4 to 5 half-lives. (The acquisition time plus delay was set > 5 T_1s.) ^{19}F resonances were integrated relative to the eighth spectrum acquired (> 4 minutes into reaction to assure temperature equilibration). Rate constants were determined by fitting the integrations to a first-order decay (integration = integration$_0$e$^{-k_{obsd}t}$ + c).

* When measuring the rate of 0.025 N solutions of PhCCLi, we used 0.0025 M solutions of **11** to maintain pseudo-first order conditions.

7-Chloro-2-methoxymethoxy-4-trifluoromethylquinazoline (11).

A 100 mL round-bottomed Schlenk flask was charged with 7-chloro-4-trifluoroquinazolin-2-one (5) (2 g, 0.008 mol), 2.1 mL of diisopropylethylamine (2.1 mL, 1.56 g, 0.012 mol), and 20 mL of dry THF. The solution was stirred under argon for one hour. Methoxymethylchloride (0.97 g, 0.012 mol) was then added and stirred for three hours with a white precipitate of diisopropylethylamine·HCl salt developing. An additional 1 mL of diisopropylethylamine was added, and the reaction was stirred for an additional hour. Filtration of the salts and evaporation of the resulting mixture afforded a yellow solid consisting of both N-protected quinazolinone and the desired O-protected quinazolinone in a 3:1 ratio. The solid was washed with 20 mL of pentane. The resultant filtrate contained the desired product, while the solid was primarily the N-protected quinazolinone. The product was then recrystallized from pentane at -78 °C to give 0.410 g of 11 (18 % yield). The product was further purified by column chromatography in 1:4 diethyl ether/hexanes and further recrystallized from pentane (100 mg 11 per 3 mL of pentane). ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.61 (s, 3H), 5.70 (s, 2H), 7.82 (dd, 1H, J = 9.0, 2.2 Hz), 7.86 (d, 1H, J = 9.0 Hz), 8.10 (br s, 1H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 58.0, 93.9, 117.7, 118.7 (q, J_{C-F} = 277.5 Hz), 123.5 (q, J_{C-F} = 2.9 Hz), 129.5, 132.6, 136.5, 152.5, 157.3 (q, J_{C-F} = 35.5 Hz), 160.2. ^{19}F NMR (470 MHz, CDCl$_3$) δ -65.3.

7-Chloro-2-methoxymethoxy-4-phenylethynyl-4-trifluoromethyl-3,4-dihydroquinzoline and 7-Chloro-2-methoxymethoxy-4-phenylethynyl-4-trifluoromethyl-1,4-dihydroquinazoline tautomers (PhCCLi adduct of 11).

A 5 mL kimble vial was charged with 11 (50 mg, 0.171 mmol) and 2 mL of dry THF. A solution of 0.60 M PhCCLi (0.5 mL, 0.3 mmol) in dry THF was added at room temperature and the reaction was complete within minutes. The solution was quenched with 1.5 mL of a sat. aq. NH$_4$Cl solution and extracted three times with 1.5 mL of diethyl ether. The organic layer was dried over NaSO$_4$, filtered, and evaporated resulting in quantitative formation of 1,4 and 3,4-dihydroquinazoline tautomers. ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.57 (s, 3H), 3.58 (s, 3H), 5.45 (d, 1H, J = 18.5 Hz), 5.46 (d, 1H, J = 18.5 Hz), 5.60 (d, 1H, J = 26.8 Hz), 5.61 (d, 1H, J = 26.8 Hz), 5.70 (br s, 1H), 6.72 (d, 1H, J = 8.5 Hz), 7.11 (d, 1H, J = 8.5 Hz), 7.20 (br s, 1H), 7.27 (dd, 1H, J = 8.5 Hz), 7.32 (dd, 1H, J = 8.5 Hz), 7.43-7.47 (m, 6H), 7.55 (m, 4H), 7.59 (br s, 1H), 7.69 (br s, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 57.9, 58.1, 59.5 (q, J_{C-F} = 33.0 Hz), 62.4 (q, J_{C-F} = 31.1 Hz), 82.5, 85.3, 86.1, 87.5, 93.1, 93.4, 115.4, 116.8, 118.0, 120.6, 121.8, 123.9 (q, J_{C-F} = 288.8 Hz), 124.4 (q, J_{C-F} = 286.8 Hz), 126.1, 127.5, 128.4, 128.5, 128.7, 129.1, 129.2, 129.3, 130.0, 130.4, 131.1, 132.2, 132.3, 134.7, 141.5, 151.7, 152.6. ^{19}F NMR (470 MHz, CDCl$_3$) δ -83.2, -81.3.

7-Chloro-4-phenylethynyl-4-trifluoromethyl-3,4-dihydroquinzolin-2-one (PhCCLi adduct of 8).

A 100 mL round-bottomed Schlenk flask was charged with 7-chloro-4-trifluoroquinazolin-2-one (5) (1 g, 0.004 mol), LiHMDS (2 g, 0.0012 mol), and 20 mL of dry THF. Phenylacetylene (0.88 mL, 0.82 g, 0.008 mmol) was added and the reaction stirred under argon for 30 minutes. The reaction was then quenched with 20 mL of a sat. aq. NH$_4$Cl solution. This solution was extracted (2 x 20 mL) with dichloromethane (CH$_2$Cl$_2$). The organic layer was washed (2 x 15 mL) with sat. aq. NaCl solution. Both aqueous layers were combined and extracted (2 x 20 mL) with CH$_2$Cl$_2$. After evaporating volatiles the product was purified by column chromatography (5 % MeOH/CH$_2$Cl$_2$, R$_f$ = 0.4). ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.98 (d, 1H, J = 8.8 Hz), 7.41-7.51 (m, 4H), 7.54 (br s, H), 7.56-7.60 (m, 2H), 8.83 (br s, 1H), 10.06 (br s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 59.5 (q, J_{C-F} = 32.1 Hz), 82.7, 87.2, 115.0, 117.1, 120.6, 124.0 (q, J_{C-F} = 289.6 Hz), 125.9, 127.8, 129.5, 130.7, 131.8, 132.5, 137.5, 151.3. ^{19}F NMR (470 MHz, CDCl$_3$) δ -80.8.

Derivation 1. Derivation of [THF] as a function of mole fraction $X_{(13)}$.

From the equilibrium expression determined experimentally:

$$[13]^2/([16][THF]^3) = K \qquad (1)$$

We define mole fraction of **13** as

$$X_{(13)} = [13]/([13] + [16]) \qquad (2)$$

or...

$$([13] + [16])X_{(13)} = [13] \qquad (3)$$

(Note: The total molarity changes with changes in the proportions of dimer **13** and tetramer **16**. The definition is still valid.)

Combining eqs 1 and 3...

$$\{([13]+[16])X_{(13)}\}^2/([16][THF]^3) = K$$

and rearranging...

$$X_{(13)}^2 = K([16][THF]^3)/([13]+[16])^2$$

$$X_{(13)} = (K[16][THF]^3)^{0.5}/([13]+[16])$$

To substitute for [16] we first define the total concentration of the lithiated quinazolinone $[8_{total}]$ as

$$[8_{total}] = [13] + 2[16]$$

$$[16] = ([8_{total}] - [13])/2$$

$$X_{(13)} = (K\{([8_{total}] - [13])/2\}[THF]^3)^{0.5}/([13]+ ([8_{total}] - [13])/2)$$

Simplify ...

$$X_{(13)} = \{K(0.5[8_{total}] - 0.5[13])[THF]^3\}^{0.5}/(0.5[13] + 0.5[8_{total}]) \qquad (4)$$

Solve for [13] by substituting for [16] from eq 1...

$$[13]^2 / (\{([8_{total}] - [13])/2\}[THF]^3) = K$$

$$2[13]^2/\{([8_{total}] - [13])[THF]^3)\} = K$$

$$[13]^2 / ([8_{total}] - [13]) = K[THF]^3/2$$

$$[\mathbf{13}]^2 = 0.5K[\text{THF}]^3[\mathbf{8}_{\text{total}}] - 0.5K[\text{THF}]^3[\mathbf{13}]$$

$$[\mathbf{13}]^2 + 0.5K[\text{THF}]^3[\mathbf{13}] - 0.5[\mathbf{8}_{\text{total}}]K[\text{THF}]^3 = 0$$

Applying the quadratic formula:

$$[\mathbf{13}] = (-0.5K[\text{THF}]^3 + ((0.5K[\text{THF}]^3)^2 + 2[\mathbf{8}_{\text{total}}]K[\text{THF}]^3)^{0.5})/2$$

Substitute for [**13**] in eq. 4 ...

$$X_{(\mathbf{13})} = (K(0.5[\mathbf{8}_{\text{total}}] - 0.5[\mathbf{13}])[\text{THF}]^3)^{0.5}/(0.5[\mathbf{13}] + 0.5[\mathbf{8}_{\text{total}}])$$

$$X_{(\mathbf{13})} = (K(0.5[\mathbf{8}_{\text{total}}] - 0.5((-0.5K[\text{THF}]^3 + ((0.5K[\text{THF}]^3)^2 + 2[\mathbf{8}_{\text{total}}]K[\text{THF}]^3)^{0.5})/2))[\text{THF}]^3)^{0.5}/(0.5((-0.5K[\text{THF}]^3 + ((0.5K[\text{THF}]^3)^2 + 2[\mathbf{8}_{\text{total}}]K[\text{THF}]^3)^{0.5})/2) + 0.5[\mathbf{8}_{\text{total}}])$$

Simplify ...

$$X_{(\mathbf{13})} = (K(0.5[\mathbf{8}_{\text{total}}] - 0.25(-0.5K[\text{THF}]^3 + ((0.5K[\text{THF}]^3)^2 + 2[\mathbf{8}_{\text{total}}]K[\text{THF}]^3)^{0.5}))[\text{THF}]^3)^{0.5}/(0.25(-0.5K[\text{THF}]^3 + ((0.5K[\text{THF}]^3)^2 + 2[\mathbf{8}_{\text{total}}]K[\text{THF}]^3)^{0.5}) + 0.5[\mathbf{8}_{\text{total}}])$$

K was determined from ...

$$-RT\ln K = \Delta H - T\Delta S$$

Derivation 2. Derivation of equation to determine reaction order via integral form, (least squares analysis).

From the nth-order expression...

$$\left(\frac{1}{[A]^{\alpha-1}} - \frac{1}{[A_0]^{\alpha-1}} \right) \frac{1}{\alpha-1} = k_{obsd}t$$

Rearranging...

$$\frac{1}{[A]^{\alpha-1}} = (\alpha-1)k_{obsd}t + \frac{1}{[A_0]^{\alpha-1}}$$

$$\frac{1}{[A]^{\alpha-1}} = \frac{(\alpha-1)[A_0]^{\alpha-1}k_{obsd}t + 1}{[A_0]^{\alpha-1}}$$

$$\frac{1}{[A]} = \frac{\left[(\alpha-1)[A_0]^{\alpha-1}k_{obsd}t + 1 \right]^{\alpha-1}}{[A_0]}$$

or...

$$[A] = \left\{ (\alpha-1)k_{obsd}t + [A_0]^{-(\alpha-1)} \right\}^{1/(\alpha-1)}$$

Let...

$$f(x) = (ax + b)^c$$

such that...

$$f(x) = [A]$$

$$x = t$$

$$a = (\alpha - 1)k_{obsd}$$

$$b = [A_0]^{-(\alpha-1)}$$

$$c = -1/(\alpha - 1)$$