

Simple ZnEt_2 as catalyst in carbodiimide hydroalkynylation: structural and mechanistic studies

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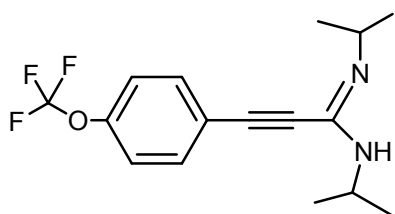
General Considerations. All reactions were performed using standard Schlenk and glove-box techniques under an atmosphere of dry nitrogen. Solvents were purified by passage through a column of activated alumina (Innovative Tech.) and degassed under nitrogen and stored over molecular sieves in the glove-box prior to use. Microanalyses were carried out with a Perkin-Elmer 2400 CHN analyzer. NMR spectra were recorded on a Varian FT-400 spectrometer using standard VARIAN-FT software. Mass spectroscopic analyses were performed on an Advion expression CMS instrument (electron impact). ZnEt_2 (1 M in hexane), ZnEt_2 (1.1 M in toluene), ZnMe_2 (2 M in toluene), alkynes, carbodiimides and isocyanates were purchased from Aldrich and used as received.

Procedure for hydroalkynylation reactions at NMR tube scale

Catalytic reactions were performed on a small scale in an NMR tube fitted with a concentric Teflon valve with 0.5 mmol of alkyne, 0.5 mmol of carbodiimide and the adequate amount of catalyst in the adequate solvent (toluene- d^8 preferentially) under nitrogen. Conversion of the starting material to product was determined by integration of the product resonances relative to the substrate peaks in the ^1H NMR spectrum. Compounds **2a-g** were identified by comparing their NMR spectra with the literature data.¹

Preparative Scale Reaction for 2a. In the glovebox, phenylacetylene (3 mL, 27 mmol) and *N,N'*-diisopropylcarbodiimide (4.2 mL, 27 mmol) in toluene (10 mL) were added in a Schlenk tube. ZnEt_2 (0.8 mmol) was then added to the above reaction mixture. The Schlenk tube was taken outside the glovebox and the reaction was stirred at 70 °C for the 24 h. Then, the solution was concentrated under reduced pressure, hexane was added and the mixture was placed in a refrigerator at -20 °C for 16 h. After filtration the product was obtained as yellowish microcrystalline solid. The mother liquor was reconcentrated in vacuo and placed in a refrigerator at -20 °C for 16 h to obtain a second crop of crystals. Total isolated yield 85%. New compound **2f** was obtained in a similar way using 4-trifluoromethoxyphenylacetylene as starting material, as a yellow solid, with an isolated yield of 88%.

2f *N,N'*-diisopropyl-3-(4-(trifluoromethoxy)phenyl)propiolimidamide



$^1\text{H NMR}$ (400 MHz, 298 K, CDCl_3) δ (ppm) = 7.51 (m, 3H, C_6H_5), 7.19 (m, 2H, C_6H_5), 3.93 (m, 2H, CH), 1.15 (d, 12H, $J = 6.2$ Hz, Me). $^{13}\text{C NMR}$ (100 MHz, 298 K, CDCl_3) δ (ppm) = 149.60, 140.68, 133.47, 120.87, 120.78, 120.20, 89.86, 80.05, 77.18, 47.18, 23.80. $^{19}\text{F NMR}$ (376 MHz, 298 K, CDCl_3) δ (ppm) -57.92. **Anal. Calcd.** for $\text{C}_{16}\text{H}_{19}\text{F}_3\text{N}_2\text{O}$: C, 61.53; H, 6.13; N, 8.97. Found, C, 61.69; H, 6.25; N, 9.01.

Synthesis of $[\text{ZnEt}\{\text{C}(\text{C}\equiv\text{CPh})(\text{N}^i\text{Pr})_2\}]_2$ **3**

To a ZnEt_2 (1 mmol) solution in toluene (5 mL), amidine **2a** (0.23 g, 1 mmol) was added. After stirring for 15 min at room temperature, the solvent was eliminated under reduced pressure and 3 mL of pentane were added. The solution was stored at -20 °C overnight affording colorless crystals of complex **3** (0.29 g, 90 %). $^1\text{H NMR}$ (400 MHz, 298 K, C_6D_6) δ (ppm) = 7.33 (m, 2H, C_6H_5), 6.96 (m, 3H, C_6H_5), 4.25 (sept, 2H, $J = 6.3$ Hz, CH), 1.67 (t, 3H, $J = 8.2$ Hz, ZnCH_2CH_3), 1.37 (d, 12H, $J = 6.3$ Hz, Me), 0.82 (2H, q, $J = 8.2$ Hz, ZnCH_2CH_3). $^{13}\text{C NMR}$ (100 MHz, 298 K, C_6D_6) δ (ppm) = 154.51 (CN_2), 131.87, 129.13, 128.29, 121.58 (C_6H_5), 96.10 ($\text{PhC}\equiv\text{C}$), 80.55 ($\text{PhC}\equiv\text{C}$), 50.80 (CH), 25.31 (CH_3), 12.87 (ZnCH_2CH_3), 4.16 (ZnCH_2CH_3). **Anal. Calcd.** for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{Zn}$: C,

63.46; H, 7.52; N, 8.71. Found, C, 63.39; H, 7.45; N, 8.60.

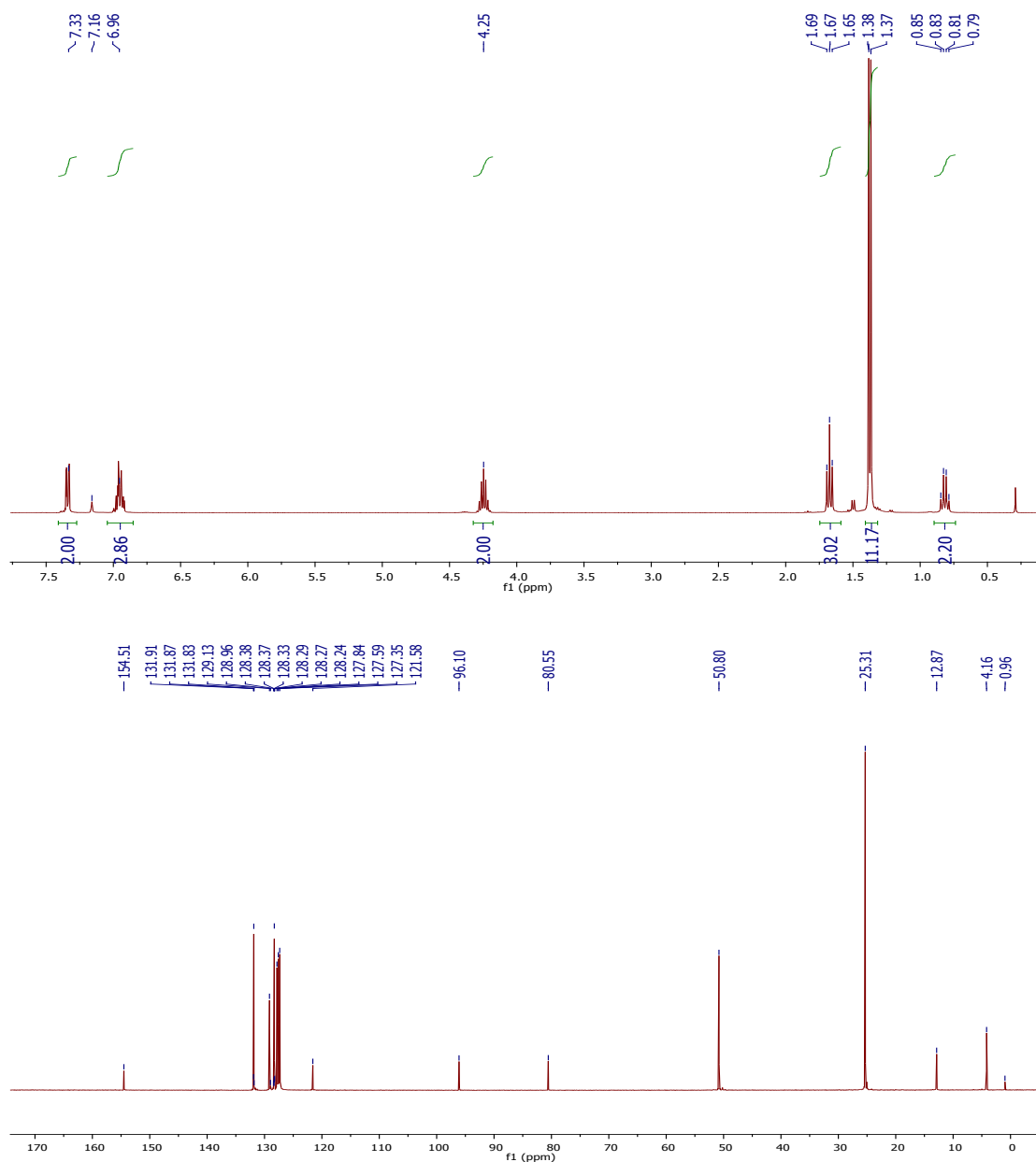


Figure S1. 1H and ^{13}C NMR spectra of **3** in C_6D_6 .

Synthesis of $[Zn\{C(C\equiv CPh)(N^iPr)_2\}_2]_2$ **4**

To a $ZnEt_2$ (1 mmol) solution in toluene (5 mL), amidine **2a** (0.43 g, 2 mmol) was added. After 2 h stirring at room temperature, the solvent was eliminated under reduced pressure and 5 mL of pentane were added. The solution was stored at $-20\text{ }^\circ C$ overnight affording light yellow crystals of complex **4** (0.49 g, 94 %). 1H NMR (400 MHz, 298 K, C_6D_6) As a mixture of dimer and monomer δ (ppm) = 7.49, 7.39, 6.94 (m, C_6H_5 , dimer and monomer), 4.45 (m, 4H, CH, dimer), 4.31 (sept, 2H, CH, monomer, $J = 6.3$ Hz), 1.68 (broad d, 12H, CH_3 , dimer), 1.56 (broad d, 12H, CH_3 , dimer), 1.36 (broad d,

12H, CH₃, monomer). ¹³C NMR (100 MHz, 298 K, C₆D₆) δ (ppm) = 158.29, 155.18, 132.30, 132.27, 132.26, 129.38, 129.31, 129.00, 128.72, 128.62, 122.92, 122.50, 122.26, 96.82, 96.10, 82.37, 81.37, 79.76, 52.62, 49.07, 48.35, 26.34, 25.70, 25.21. **Anal Calcd** for C₃₀H₃₈N₄Zn: C, 69.29; H, 7.37; N, 10.77. Found, C, 70.01; H, 7.41; N, 10.82.

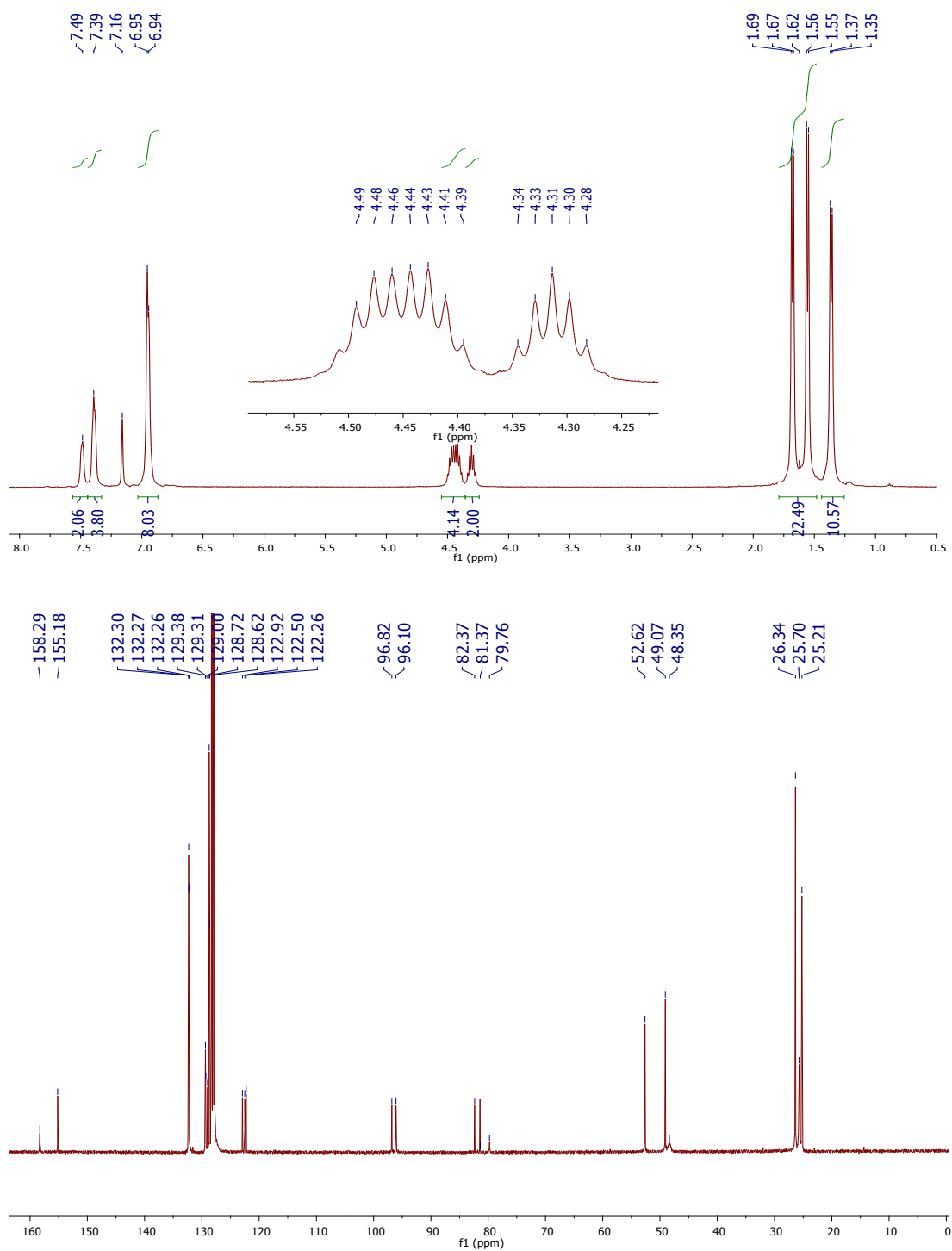


Figure S2. ¹H and ¹³C NMR spectra of **4** in C₆D₆.

Van't Hoff analysis for the dimer-monomer equilibrium found in compound **4**

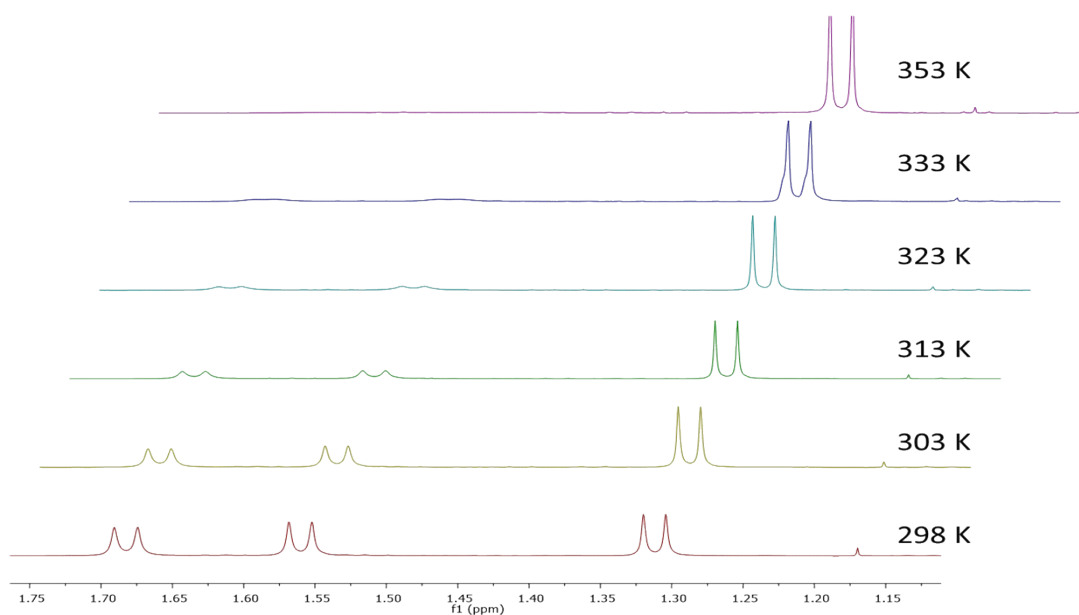


Figure S3. ¹H NMR spectra (isopropyl zone) of **4** in C₆D₆ at different temperatures.

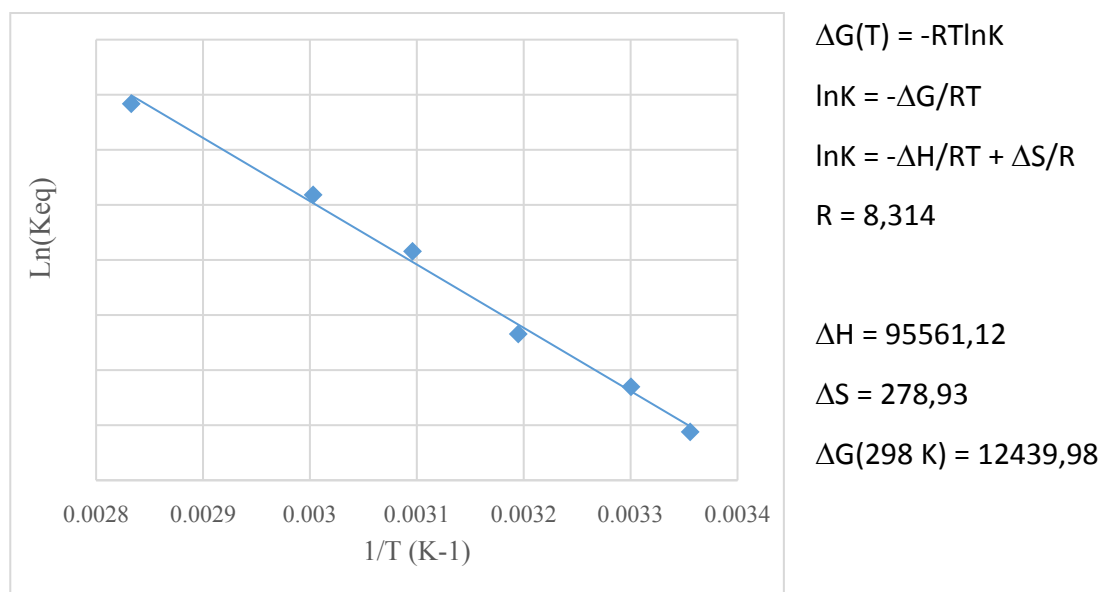


Figure S4. Van't Hoff analysis.

Synthesis of [Zn{C(C≡CPh)(NⁱPr)(NHⁱPr)}₂(C≡CPh)₂] **5**

Phenylacetylene (62 μl, 0.60 mmol) was added to a toluene solution (5 mL) of compound **4** (0.150 g, 0.29 mmol). After stirring for 15 min at room temperature, the solution was concentrated under reduced pressure and 3 mL of pentane were added and the reaction mixture was kept at -20 °C for 16 h, affording colourless crystals of complex

5 (0.085 g, 40 %). Partial spectroscopic data from **5** solutions (see the text): ^1H NMR (400 MHz, 298 K, C_6D_6) δ (ppm) = 9.05 (bs, NH), 7.9-6.9 (m, C_6H_5), 4.45 (sept, CH, $J = 6.5$ Hz), 4.24 (m, CH), 2.00-1.35 (bs, CH_3), 1.45 (d, CH_3 , $J = 6.5$ Hz). Anal Calcd for $\text{C}_{46}\text{H}_{50}\text{N}_4\text{Zn}$: C, 76.28; H, 6.96; N, 7.74 Found, C, 75.99; H, 6.90; N, 7.68.

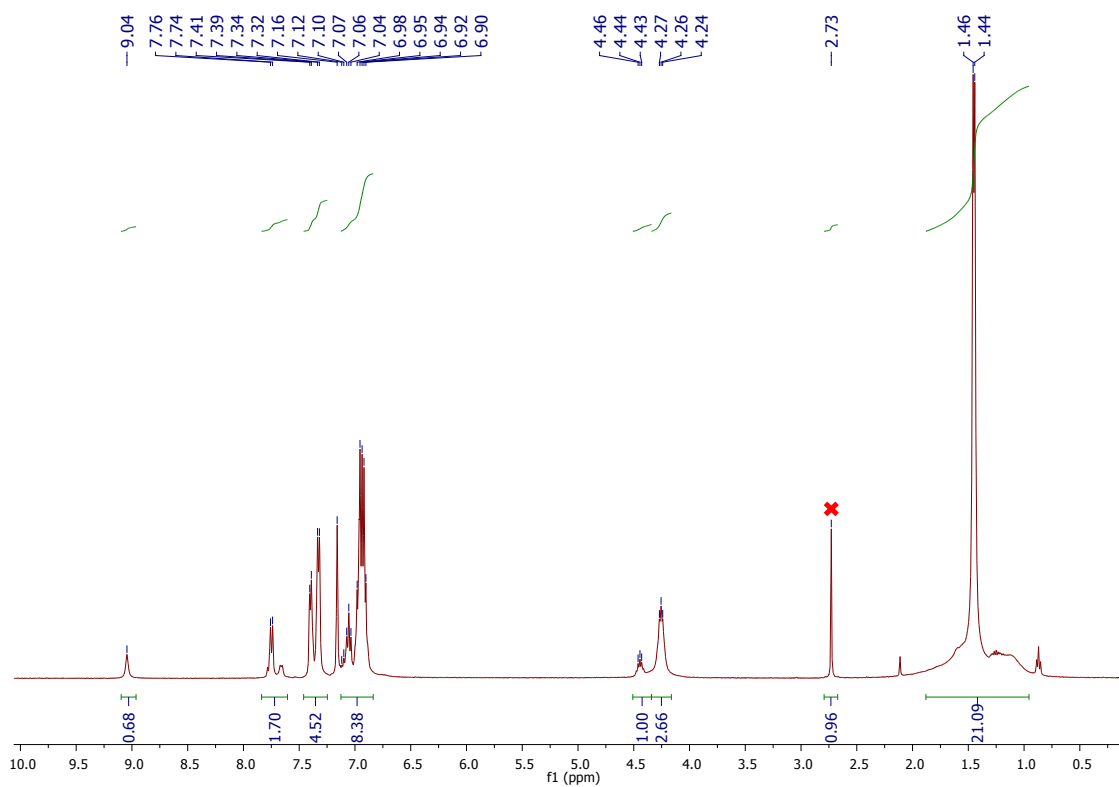


Figure S5. ^1H NMR spectrum of **5** in C_6D_6 . **x**: CH from free alkyne.

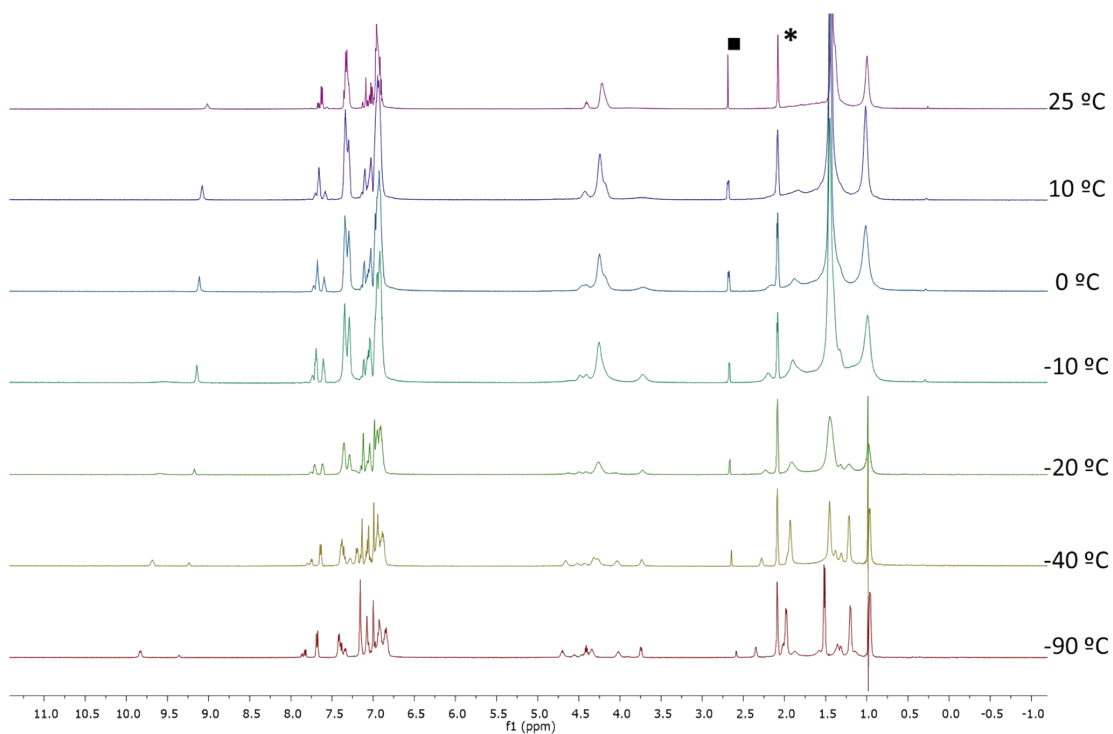


Figure S6. Variable temperature ^1H NMR experiment in toluene- d^8 solutions of **5**.

* solvent, ■ free PhCCH.

General procedure for kinetic experiments

Kinetic experiments were performed using a Varian FT-400 MHz spectrometer. A standard solution 0.11M of catalyst **1** was made, obtained from a 1.1 M solution in toluene and diluted in deuterated toluene. The described kinetic experiments were carried out on the *N,N'*-disopropylcarbodiimide and phenylacetylene (or deuterated phenylacetylene) to form the corresponding propiolamidine **2a**.

The reactions were carried out in J-Young NMR tubes and the reaction rates were measured by monitoring the disappearance of carbodiimide (or alkyne) relative to the internal standard tetrakis(trimethylsilyl)silane (6 mg) by ^1H NMR spectroscopy at the described intervals over more than three half-lives. All data were processed using Varian integral analysis software. Reaction rates were derived by fitting data to zero, first or second order equations by using linear trend lines generated by Microsoft Excel software.

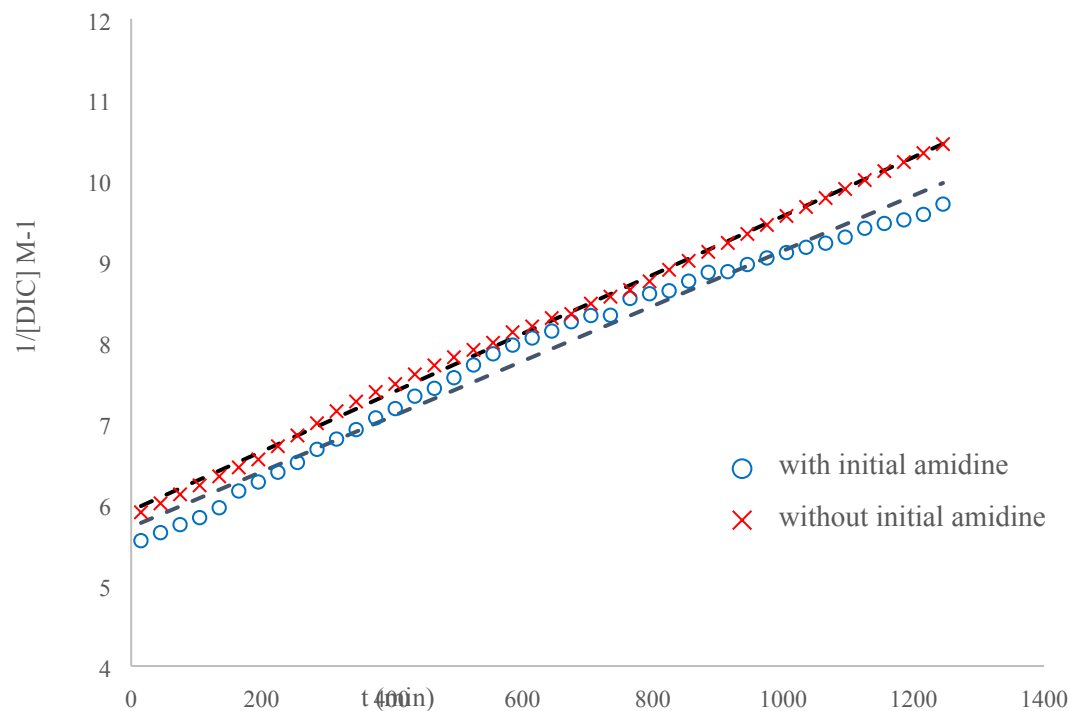


Figure S7. Effect of the initial amidine concentration on the kinetic behaviour. $[DIC]_0 = [PhCCH]_0 = 0.23M$, $[amidine]_0 = 0.12 M$, $[1] = 6.8 \cdot 10^{-3}M$.

Procedure for isocyanate insertion and hydroamination reactions at NMR tube scale

Catalytic reactions were performed on a small scale in an NMR tube fitted with a concentric Teflon valve with 0.5 mmol of alkyne, 0.5 mmol of carbodiimide and $ZnEt_2$ (3% mol) in toluene- d_8 under nitrogen, at 70° C for 24h. Then 0.5 mmol of the corresponding isocyanate or isothiocyanate were added to the NMR tube inside the glovebox, and the mixture heated at 70° C for 24 h. Compounds **6a**, **d**, **g** were identified by comparing their NMR spectra with the literature data.^{1e}

6b, 1H NMR (400 MHz, toluene- d_8) δ (ppm) 7.37-6.57 (m, C_6H_5), 5.36 (m, CH, Cy), 5.14 (m, CH, Cy), 4.58 - 1.06 (m, Cy). MS (ESI) (m/z): 428 ($M^+ + H^+$).

6c, 1H NMR (400 MHz, toluene- d_8) δ (ppm) 7.02-6.74 (m, C_6H_5), 3.80 (q, CH_2 , $J = 7.1$ Hz), 1.59 (s, *t*Bu), 1.25 (t, CH_3 , $J = 7.1$ Hz). MS (ESI) (m/z): 348 ($M + H^+$).

6e, 1H NMR (400 MHz, toluene- d_8) δ (ppm) 8.41-6.52 (m, C_6H_5), 4.35 (m, CH, *i*Pr), 4.22 (m, CH, *i*Pr), 1.90 (s, CH_3 , tosyl), 1.21 (d, CH_3 , *i*Pr, $J = 7.0$ Hz), 0.99 (d, CH_3 , *i*Pr, $J = 7.0$ Hz). MS (ESI) (m/z): 426 ($M + H^+$).

6f, ^1H NMR (400 MHz, toluene- d^8) δ (ppm) 7.10-6.51 (m, C_6H_5), 4.87 (m, CH, *i*Pr), 4.30 (m, CH, *i*Pr), 1.99 (s, CH_3 , xylyl), 1.50 (d, CH_3 , *i*Pr, $J = 7.0$ Hz), 1.23 (d, CH_3 , *i*Pr, $J = 7.0$ Hz). MS (ESI) (m/z): 376 ($\text{M}+\text{H}^+$).

6h, ^1H NMR (400 MHz, toluene- d^8) δ (ppm) 7.00-6.35 (m, C_6H_5), 4.85 (m, CH, *i*Pr), 4.35 (m, CH, *i*Pr), 1.50 (d, CH_3 , *i*Pr, $J = 7.0$ Hz), 1.33 (d, CH_3 , *i*Pr, $J = 7.0$ Hz). ^{19}F NMR (376 MHz, toluene- d^8) δ (ppm) -114.37. MS (ESI) (m/z): 366 ($\text{M}+\text{H}^+$).

6i, ^1H NMR (400 MHz, toluene- d^8) δ (ppm) 7.20-6.50 (m, C_6H_5), 4.83 (m, CH, *i*Pr), 4.35 (m, CH, *i*Pr), 1.47 (d, CH_3 , *i*Pr, $J = 7.0$ Hz), 1.33 (d, CH_3 , *i*Pr, $J = 7.0$ Hz). ^{19}F NMR (376 MHz, toluene- d^8) δ (ppm) -62.85. MS (ESI) (m/z): 416 ($\text{M}+\text{H}^+$).

6j, ^1H NMR (400 MHz, toluene- d^8) δ 6.69-6.41 (m, C_6H_5), 4.85 (m, CH, *i*Pr), 4.34 (m, CH, *i*Pr), 1.48 (d, CH_3 , *i*Pr, $J = 6.6$ Hz), 1.33 (d, CH_3 , *i*Pr, $J = 6.6$ Hz). ^{19}F NMR (376 MHz, toluene- d^8) δ (ppm) -58.19. MS (ESI) (m/z): 432 ($\text{M}+\text{H}^+$).

6k, ^1H NMR (400 MHz, toluene- d^8) δ 7.27-6.31 (m, C_6H_5), 4.88 (m, CH, *i*Pr), 4.41 (m, CH, *i*Pr), 3.20 (s, OCH_3), 1.49 (d, CH_3 , *i*Pr, $J = 6.7$ Hz), 1.35 (d, CH_3 , *i*Pr, $J = 6.6$ Hz). MS (ESI) (m/z): 378 ($\text{M}+\text{H}^+$).

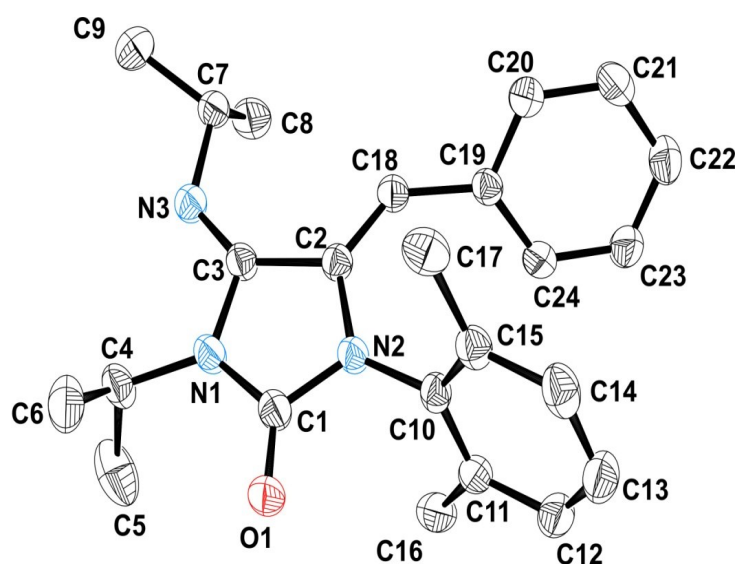
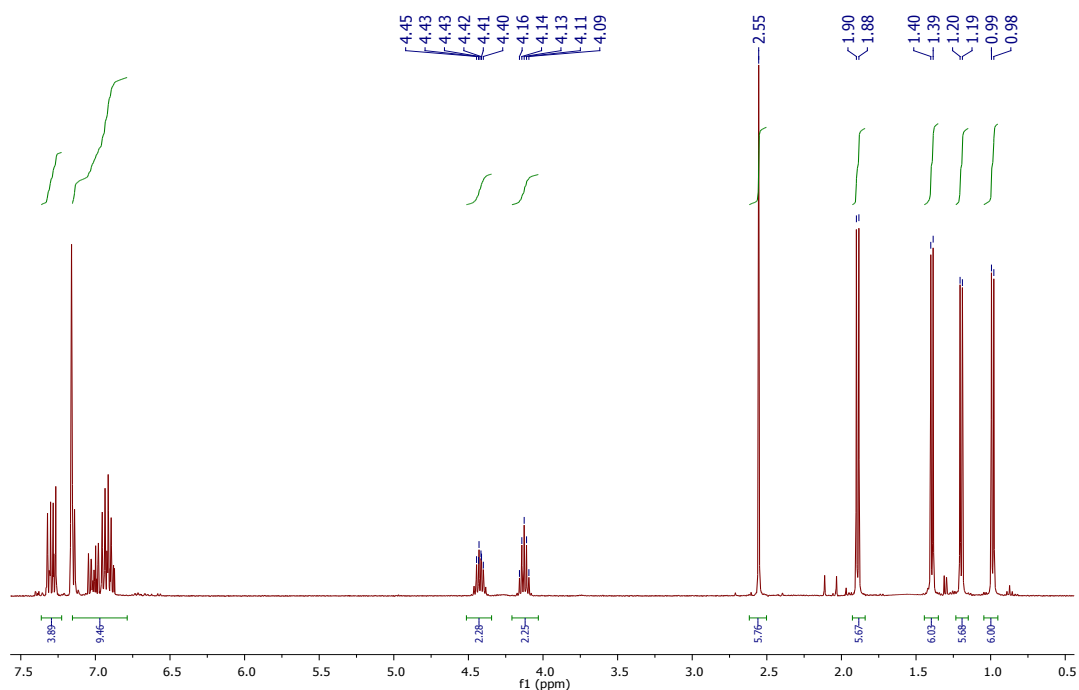


Figure S8. ORTEP drawing of compound **6f**. Hydrogen atoms are omitted for clarity and thermal ellipsoids are shown at 30% probability.

Synthesis of $[\text{Zn}\{\text{C}(\text{C}\equiv\text{CPh})(\text{N}^i\text{Pr})_2\}\{\text{N}(2,6\text{-Me}_2\text{C}_6\text{H}_3)(\text{CO})(\text{N}^i\text{Pr})\text{C}(\text{C}\equiv\text{CPh})(\text{N}^i\text{Pr})\}]$ 7. 2,6-Me₂C₆H₃NCO (54 μl, 0.38 mmol) was added to a toluene solution (5 mL) of compound 4 (0.20 g, 0.38 mmol). After stirring for 15 min at room temperature, the solution was concentrated under reduced pressure and 5 mL of hexane were added and the mixture was placed in a refrigerator at -20 °C for 16 h, affording colorless microcrystals of complex 7 (0.24 g, 95%). ¹H NMR (400 MHz, 298 K, C₆D₆) δ (ppm) = 7.33-6.87 (m, 13H, C₆H₅, C₆H₃), 4.42 (m, 2H, CH), 4.13 (m, 2H, CH), 2.55 (s, 6H, Me₂C₆H₃), 1.89 (d, 6H, CH₃, J = 6.5 Hz), 1.39 (d, 6H, CH₃, J = 6.6 Hz), 1.19 (d, 6H, CH₃, J = 6.6 Hz), 0.98 (d, 6H, CH₃, J = 6.3 Hz). ¹³C NMR (100 MHz, 298 K, C₆D₆) δ (ppm) = 156.03, 155.13, 148.83, 146.09, 133.77, 132.36, 132.23, 130.62, 129.37, 128.91, 128.60, 128.51, 128.13, 127.88, 124.05, 122.03, 120.50, 100.20, 97.15, 54.87, 54.57, 47.62, 26.13, 25.59, 24.21, 22.20, 19.42. **Anal Calcd** for C₃₉H₄₇N₅OZn: C, 70.21; H, 7.10; N, 10.50 Found, C, 70.25; H, 7.16; N, 10.58.



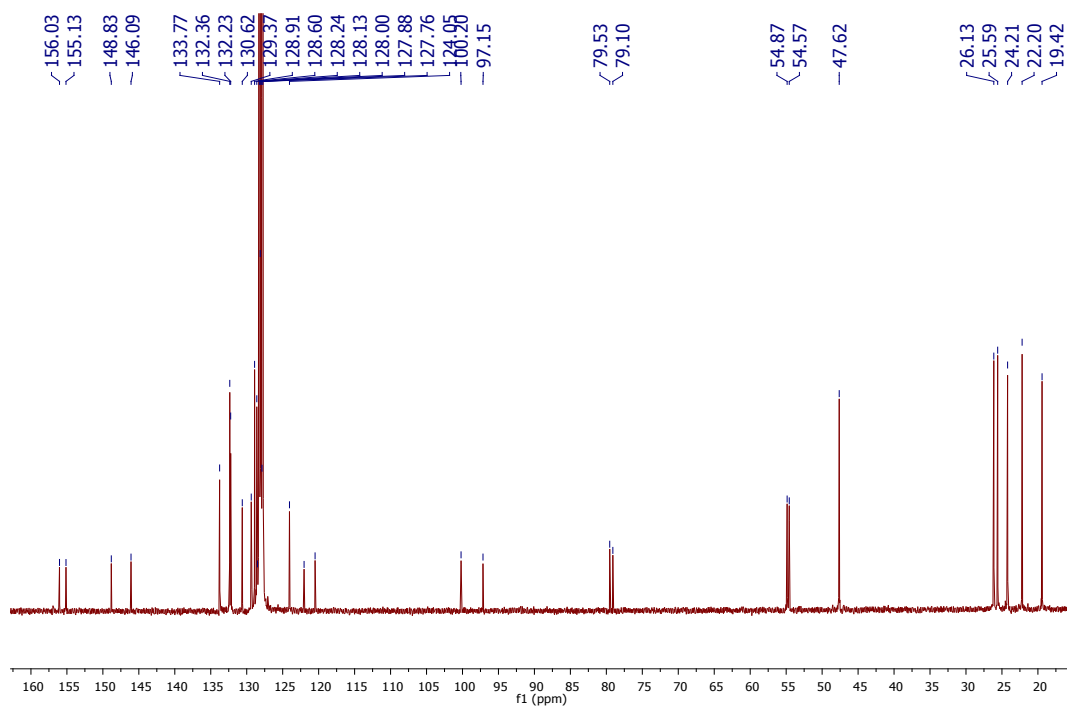


Figure S9. ^1H and ^{13}C NMR spectra of **7** in C_6D_6 .

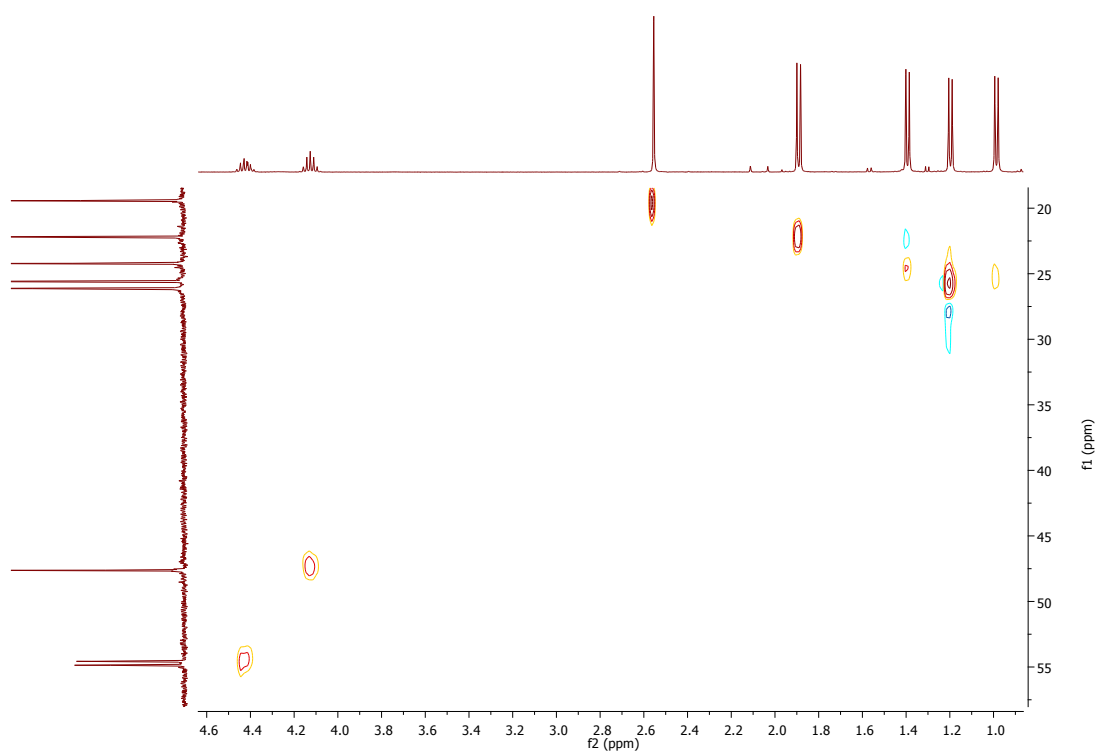


Figure S9. gHSQC NMR experiment of **7** in C_6D_6 .

Table S1. Crystallographic data and structure refinement details of all compounds.

Compound	3	4	5	6f	7
Chem. form.	C ₃₄ H ₄₈ N ₄ Zn ₂	C ₅₉ H ₇₆ N ₉ Zn ₂	C ₄₆ H ₅₀ N ₄ Zn	C ₂₄ H ₂₉ N ₃ O	C ₃₉ H ₄₇ N ₅ OZn
CCDC	1554604	1554605	1554606	1554608	1554607
Form. weight	643.50	1042.02	724.27	375.50	667.18
Cryst. system	Triclinic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	<i>P</i> -1	<i>C</i> 2/ <i>c</i>	<i>C</i> 2/ <i>c</i>	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ 2 ₁ 2 ₁
<i>a</i> (Å)	9.1553(4)	36.640(10)	10.358(2)	11.241(2)	9.3796(8)
<i>b</i> (Å)	13.1015(6)	9.4509(10)	19.359(3)	9.865(2)	15.6315(13)
<i>c</i> (Å)	15.1781(14)	34.379(6)	20.131(3)	19.417(4)	24.742(2)
α (°)	75.6480(10)	90	90	90	90
β (°)	73.4920(10)	98.993(11)	100.144(4)	94.000(3)	90
γ (°)	78.631(2)	90	90	90	90
<i>V</i> (Å ³)	1675.26(19)	11758(4)	3973.6(12)	2147.9(8)	3627.5(5)
<i>Z</i>	2	8	4	4	4
GOF ^a	1.094	1.025	1.050	0.948	1.026
<i>R</i> _{int}	0.0371	0.0819	0.0917	0.0687	0.1577
<i>R</i> ₁ ^b / <i>wR</i> ₂ ^c [<i>I</i> > 2σ(<i>I</i>)]	0.0228 / 0.0572	0.0548 / 0.1370	0.0348 / 0.0676	0.0520 / 0.1234	0.0706 / 0.1466
<i>R</i> ₁ ^b / <i>wR</i> ₂ ^c (all data)	0.0287 / 0.0601	0.0812 / 0.1561	0.0523 / 0.0735	0.1163 / 0.1517	0.1177 / 0.1732

$$[a] S = [\sum w(F_o^2 - F_c^2)^2 / (N_{obs} - N_{param})]^{1/2} [b] R_1 = \sum ||F_o| - |F_c|| / \sum |F_o| [c] wR_2 = [\sum w(F_o^2 - F_c^2)^2 / \sum wF_o^2]^{1/2}$$

$$w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP] \text{ where } P = (\max(F_o^2, 0) + 2F_c^2)/3$$

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