

SUPPLEMENTARY MATERIAL FOR:
Novel synthesis of isoquinolines using isobenzofuran-nitrile
Diels-Alder reactions

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General Procedure 1: Synthesis of Carbene Complexes 4a-c: To a solution of carbene complex **1a-c** (1 mmol) in ether (20 mL) was added *n*-butyllithium (1 mmol) at -78 °C. After 0.5 h this solution was added to a solution of bromoacetonitrile (10 mmol) in THF (20 mL) at 0 °C by means of canula. Mixture was stirred for 2 h at 0 °C. The solvent was removed in a rotary evaporator. Column chromatography of the crude product over silica gel gave product **4a-c**. Complexes **4a-c** were quite unstable and were used within a few hours after purification.

Synthesis of Carbene Complex 4a: General Procedure 1 was followed using carbene complex **1a** (0.400 g, 1.6 mmol), *n*-butyllithium (2.9 mL of a 1.4M hexane solution, 4.0 mmol) and bromoacetonitrile (0.28 mL, 4.0 mmol). Purification using column chromatography (silica gel, hexane/ ethyl acetate, 3:1) gave **4a** (0.400 g, 46% yield) contaminated by 5-10% of bromoacetonitrile. ¹H NMR (CDCl₃): δ 4.90 (s, 3 H), 4.50 (quintet, 1 H, J = 6.6 Hz), 2.65 (dd, 2 H, J = 17.4, 6.6 Hz), 2.58 (dd, 2 H, J = 17.4, 6.6 Hz); ¹³C NMR (CDCl₃): δ 353.9, 222.6, 215.8, 116.5, 69.0, 59.3, 19.3; IR (neat): 2259, 2066, 1919, 1454 cm⁻¹.

Synthesis of Carbene Complex 4b: General Procedure 1 was followed using carbene complex **1b** (0.30 g, 0.92 mmol), ¹ *n*-butyllithium (0.44 mL of a 1.6M hexane solution, 0.70 mmol) and bromoacetonitrile (0.85 g, 0.71 mmol). Purification using column chromatography (silica gel, hexane/ ethyl acetate, 4:1) gave **4b** (0.14 g, 88% yield) and starting material **1b** (0.16 g). ¹H NMR (CDCl₃): δ 4.70 (s, 3 H), 4.45 (m, 1 H), 2.45-2.78 (m, 4 H), 1.60-1.78 (m, 6 H), 1.25-1.55 (m, 12 H), 0.97 (br t, 9 H, J = 6.8 Hz); ¹³C NMR (CDCl₃): δ 338.6(d), 222.2, 221.9, 116.8, 64.6, 58.3, 27.8 (d), 25.4, 24.3 (d), 18.8, 13.6; IR (neat): 2235, 2008, 1883 cm⁻¹.

Synthesis of Carbene Complex 4c: General Procedure 1 was followed using carbene complex **1c** (0.52 g, 1.78 mmol), *n*-butyllithium (1.1 mL of a 1.6M hexane solution, 1.76 mmol) and bromoacetonitrile (2.14 g, 17.8 mmol). Purification using column chromatography (silica gel, hexane/ ethyl acetate, 9:1) gave **4c** (0.310 g, 52%). ¹H NMR (CDCl₃): δ 4.849 (s, 3 H), 4.22 (m, 1 H), 2.39 (t, 1 H, J = 6.5 Hz), 1.2-1.8 (m, 5 H), 0.95 (t, 3 H, J = 6.5 Hz); IR(neat): 2240, 2063, 1919 cm⁻¹.

¹ Xu, Yao Chang; Wulff, William D. *J. Org. Chem.* **1987**, 52, 3263-3275.

General Procedure 2: Synthesis of Carbene Complexes 4d and 6a: ² 1) *Preparation of Dipotassium Pentacarbonylchromate:* Graphite (64 eq) was heated at 150 °C – 160 °C while being stirred under argon for 2 h. The graphite was cooled to room temperature and potassium (8 eq) was added as tiny pieces under a positive flow of argon. The mixture was heated to 160 °C with stirring for 1 h. THF was added to the bronze colored material and cooled to –78 °C. Chromium hexacarbonyl (3.5 eq) was then added under a positive flow of argon. The reaction mixture was stirred for 30 min at –78 °C and placed in an ice bath until a thick slurry of product was formed. This mixture was directly used in the next step. 2) *Preparation of tetramethylammonium salt of the chromium carbene complex.* To the solution of dipotassium pentacarbonylchromate in THF at –78 °C obtained from step 1, the acid chloride (1 eq) in THF was added dropwise. The resulting mixture was stirred at –78 °C for 15 min, at 0 °C for 1.5 h, and at room temperature for 1 h. The solvent was removed under reduced pressure. Cold water was added to the residue and filtered through Celite. To the filtrate was added a saturated aqueous solution of tetramethylammonium bromide, leading to immediate precipitation of the ammonium salt. The precipitate was removed by extracting the aqueous layer with dichloromethane. The organic layer was then dried over anhydrous sodium sulfate and the solvent was removed on a rotary evaporator to give a pale yellow solid. 3) *Alkylation of tetramethylammonium acylate salt.* To a solution of the ammonium salt (1 eq) in dichloromethane obtained in step 2, methyl triflate (1.2 eq) was added at 0 °C. The reaction mixture was then stirred at 0 °C for 0.5 h and at room temperature for 1 h. The mixture was filtered through Celite, washed with saturated aqueous sodium bicarbonate solution, water, brine, and dried over sodium sulfate. The solvent was removed on a rotary evaporator to yield the carbene complex. Purification was done by flash column chromatography using hexane-ethyl acetate (4:1) as the eluting solvent. Both of these complexes were highly unstable and used within a few hours after purification.

Synthesis of Carbene Complex 4d: General Procedure 2 was followed using dipotassium pentacarbonylchromate (prepared from graphite [2.34 g, 195 mmol], potassium metal (0.95 g, 24.3 mmol), and chromium hexacarbonyl (2.42 g, 11.0 mmol)], *cis* 2-cyanocyclohexanecarbonyl chloride (0.55 g, 3.2 mmol),³ and methyl triflate (0.63 g, 3.84 mmol). The crude product was purified by flash chromatography to give **4d**, dark yellow solid (0.670 g, 61%). ¹H NMR (CDCl₃): δ 4.90 (s, 3 H), 3.96 (m, 1 H), 3.08 (m, 1 H), 1.58-2.20 (m, 6 H), 1.25-2.20 (m, 6 H), 1.25-1.58 (m, 2 H); ¹³C NMR (CDCl₃): δ 358.3, 215.6, 214.2, 130.8, 69.6, 68.2, 30.6, 29.6, 25.6, 24.8, 22.0; IR(neat): 2264, 2063, 1919 cm⁻¹.

² This is a variant of a literature procedure: Schwindt, M..A.; Lejon, T.; Hegedus, L.S. *Organometallics* **1990**, 9, 2814-2819. This procedure is very reliable if one is careful to cut the potassium into small pieces and if the tetramethylammonium acylate salt is prepared prior to the alkylation step. Otherwise we noted wide variances in the yields between different experimental runs.

³ Prepared from *cis* 1,2-cyclohexanedicarboxylic anhydride via amide formation (treatment with aqueous ammonia), followed by amide dehydration (acetic anhydride), followed by acid chloride formation (oxalyl chloride)

Synthesis of Carbene Complex 6a: General Procedure 2 was followed using dipotassium pentacarbonylchromate [prepared from graphite (2.34 g, 195 mmol), potassium metal (0.95 g, 24.3 mmol) and chromium hexacarbonyl (2.42 g 11.0 mmol)], acid chloride **5a** (0.53 g, 3.2 mmol), and methyl triflate (0.63 g, 3.84 mmol). The crude product was purified by passage through a short silica gel column to give **6a** (0.378 g, 35% yield) and was immediately used for next step as it is an unstable compound.

¹H NMR (CDCl₃) (poorly resolved): δ 7.52-7.80 (m, 2 H), 7.30-7.50 (m, 2 H), 4.95 (s, 3 H); IR: 2068, 1930 cm⁻¹.

General Procedure 3: Synthesis of Carbene Complexes 4e and 6b: To the solution of dipotassium pentacarbonylchromate (prepared using general procedure 2, step 1) in THF at -78 °C, the amide (1 eq) in THF was added dropwise. The resultant mixture was stirred at -78 °C for 0.5 h, warmed to 0 °C for 1 h, and cooled to -78 °C.

Chlorotrimethylsilane (3 eq) was then added. After 0.5 h, the mixture was warmed to room temperature. Neutral Al₂O₃ (2.5 g/ 1mmol of amide) was added to absorb the product, and the solvent was removed under reduced pressure. The resulting dry powder was chromatographed on a silica gel column with hexane-dichloromethane (1:1) as eluent.

Synthesis of Carbene Complex 4e: General Procedure 3 was followed using dipotassium pentacarbonylchromate [prepared from graphite (1.78 g, 148 mmol), potassium metal (0.72 g, 18.5 mmol) and chromium hexacarbonyl (2.42 g 8.4 mmol)], cis N,N-dimethyl-2-cyanocyclohexanecarboxamide (0.82 g, 4.55 mmol),⁴ and chlorotrimethylsilane (1.50 g, 14.0 mmol). The crude product was purified by flash chromatography to give **4e** (0.650 g, 40%). ¹H NMR (CDCl₃): δ 3.98 (s, 3 H), 3.93 (br s, 1 H), 3.55 (s, 3 H), 3.29 (bs, 1 H), 1.3-2.3 (m, 8 H); ¹³C NMR (CDCl₃): δ 280.0, 217.2, 213.8, 131.1, 62.0, 56.1, 46.7, 31.7, 31.3, 28.2, 26.2, 22.3; IR (neat): 2053, 1903 cm⁻¹.

Synthesis of Carbene Complex 6b: General Procedure 3 was followed using dipotassium pentacarbonylchromate [prepared from graphite (2.34 g, 195 mmol), potassium metal (0.95 g, 24.3 mmol) and chromium hexacarbonyl (2.42 g 11.0 mmol)], amide **5b**⁵ (1.04 g, 6.0 mmol) and chlorotrimethylsilane (1.95 g, 18.0 mmol). The crude product was purified by flash chromatography to give **6b** (1.35 g, 64%). ¹H NMR (CDCl₃): δ 7.55-7.78 (m, 2 H), 7.34 (d, 1 H, J = 8 Hz), 6.95 (d, 1 H, J = 8 Hz), 4.13 (s, 3 H), 3.19 (s, 3 H); ¹³C NMR (CDCl₃): δ 272.3, 216.1, 213.8, 154.7, 134.0, 133.0, 126.7, 121.4, 100.6, 51.4, 46.4; IR(neat): 2057, 1918 cm⁻¹.

⁴ Prepared from reaction of the acid chloride (footnote 3) with aqueous dimethylamine.

⁵ Armarego, W.L.F.; Sharma, S.C. *J. Chem. Soc. C* **1970**, 1600-1606.

General Procedure 4: Coupling of β -cyanocarbene Complexes (4,6) with *o*-alkynyl benzaldehyde/ *o*-alkynyl acetophenones (2): To a refluxing solution of 1.0 eq of *o*-alkynyl benzaldehyde/ *o*-alkynyl acetophenone (2) in a minimum volume of dioxane under argon was added dropwise a 0.05M solution of carbene complex (1.1 eq) in dioxane over a 2h period. After the addition was complete, the mixture was allowed to reflux for a period of 16-24 h. The reaction mixture was cooled to room temperature and concentrated on a rotary evaporator. Ethyl acetate (25mL) was added and the residue was filtered through Celite. The solvent was removed on a rotary evaporator and the crude products were purified by flash column chromatography.

Coupling of Carbene Complex 4a with 2-hex-1-ynylbenzaldehyde (2a) (Entry A): General Procedure 4 was followed using carbene complex **4a** (100 mg, 0.30 mmol) and 2-hex-1-ynylbenzaldehyde (**2a**) (60 mg, 0.32 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (1:1) as eluent to yield products **7a** (36 mg, 40%), **8** (29 mg, 36%), and a compound tentatively identified as enol ether **9** (5 mg, 13%, yield varies widely between experimental runs). *Compound 7a:* ^1H NMR (CDCl_3): δ 8.99 (s, 1 H), 8.09 (d, 1 H, J = 8.4 Hz), 7.94 (d, 1 H, J = 8.4 Hz), 7.67 (t, 1 H, J = 7.5 Hz), 7.55 (t, 1 H, J = 7.5 Hz), 3.84 (s, 3 H), 3.45 (m, 1 H), 3.00-3.30 (m, 2 H), 2.65-3.00 (m, 2 H), 2.18-2.5 (m, 2 H), 1.10-1.50 (m, 4 H), 0.80 (t, 3 H, J = 7 Hz); ^{13}C NMR (CDCl_3): δ 156.8, 148.4, 144.6, 133.0, 130.5, 128.8, 128.3, 126.7, 124.5, 118.4, 118.1, 58.1, 36.6, 31.0, 30.4, 28.2, 22.5, 18.8, 13.7; IR (neat): 2239, 1615, 1551 cm^{-1} ; MS: (m/e) 307 (M^++1 , 13), 306 (M^+ , 55), 291 (M^+-CH_3 , 10), 266 (45), 210 (100), 180 (21), 167 (24). HRMS: Calcd. For $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}$ is 306.17322, found 306.17373. *Compound 8:* ^1H NMR (CDCl_3): δ 9.10 (br s, 1 H), 8.69 (d, 1 H, J = 8.4 Hz), 8.12 (d, 1 H, J = 9.0 Hz), 8.04 (d, 1 H, J = 7.7 Hz), 7.84 (t, 1 H, J = 7.3 Hz), 7.71 (t, 1 H, J = 7.3 Hz), 7.44 (d, 1 H, J = 9.0 Hz), 4.01 (s, 3 H), 3.35 (t, 2 H, J = 8.0 Hz), 1.75-1.98 (m, 2 H), 1.50-1.75 (m, 2 H), 1.09 (t, 3 H, J = 7.5 Hz); ^{13}C NMR (CDCl_3): δ 157.1, 150.8, 139.8, 133.2, 130.3, 129.2, 128.8, 127.3, 127.0, 126.6, 113.3, 56.4, 30.8, 28.2, 23.2, 13.9; IR (neat): 2957, 2871, 1616, 1495 cm^{-1} ; MS: (m/e) 267 (M^++2 , 6), 266 (M^++1 , 26), 265 (M^+ , 54), 222 (100), 206 (5), 191 (7), 179 (29), 152 (7); HRMS: Calcd. For $\text{C}_{18}\text{H}_{19}\text{NO}$ is 265.146664, found 265.145879. *Compound 9:* ^1H NMR (CDCl_3): δ 6.40 (br s, 1 H); 3.73 (s, 3 H), 3.28 (s, 2 H), 3.14 (s, 2 H); IR (neat): 2248 (m), 1652 (s) cm^{-1} .⁶

Coupling of Carbene Complex 4b with 2-hex-1-ynyl-benzaldehyde (2a) (Entry B): General Procedure 4 was followed using carbene complex **4b** (0.165 g, 0.33 mmol) and 2-hex-1-ynylbenzaldehyde (**2a**) (0.056 g, 0.30 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (1:1) as eluent to yield products **7a** (0.044 g, 48%) and **8** (0.015 g, 19%).

Coupling of Carbene Complex 4c with 2-hex-1-ynyl-benzaldehyde (2a) (Entry C): General Procedure 4 was followed using carbene complex **4c** (0.150 g, 0.45 mmol) and

⁶ This compound is known however the spectral data is inaccessible: *Chem. Abstr.* **1976**, 86, 189240.

2-hex-1-ynyl-benzaldehyde (**2a**) (0.075 g, 0.40 mmol); in this experiment triphenylphosphine (0.118 g, 0.45 mmol) was added and toluene was used as the solvent (in place of dioxane). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (4:1) as eluent to yield product **12c** (0.065 g, 53%). ¹H NMR (CDCl₃): δ 9.15 (s, 1 H), 8.71 (d, 1 H, J = 8 Hz), 8.04 (d, 1 H, J = 8.0 Hz), 7.96 (s, 1 H), 7.83 (t, 1 H, J = 7.7 Hz), 7.68 (t, 1 H, J = 7.7 Hz), 3.85 (s, 3 H), 3.43 (t, 2 H, J = 8.0 Hz), 2.87 (t, 2 H, J = 7.7 Hz), 1.70-1.93 (m, 4 H), 1.52-1.70 (m, 2 H), 1.05 (t, 3 H, J = 7.3 Hz), 1.03 (t, 3 H, J = 7.3 Hz); ¹³C NMR (CDCl₃): δ 156.8, 152.4, 142.8, 137.3, 133.3, 132.4, 130.3, 129.5, 129.3, 127.3, 126.5, 126.0, 122.4, 61.6, 32.4, 31.8, 28.7, 23.2 (2C), 14.2, 13.9; IR (neat): 2958, 2871, 1591, 1446 cm⁻¹; MS: (m/e) 309 (M⁺+2, 3), 308 (M⁺+1, 20), 307 (M⁺, 59), 292 (M⁺-CH₃, 4), 264 (100), 234 (16), 222 (9), 204 (9), 192 (13), 165 (5); HRMS: Calcd. For C₂₁H₂₅NO is 307.193615, found 307.194478

Coupling of Carbene Complex **4c** with 2-ethynylbenzaldehyde (**7d**) (Entry D):

General Procedure 4 was followed using carbene complex **4c** (0.345 g, 1.0 mmol) and 2-ethynylbenzaldehyde (**7d**) (0.117 g, 0.90 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (4:1) as eluent to yield product **7d** (0.050 g, 21%). ¹H NMR (CDCl₃): δ 8.97 (s, 1 H), 8.01 (d, 1 H, J = 8.0 Hz), 7.92 (d, 1 H, J = 8.0 Hz), 7.68 (t, 1 H, J = 7.5 Hz), 7.53 (t, 1 H, J = 7.5 Hz), 6.08 (s, 1 H), 3.57 (s, 3 H), 3.45 (br s, 1 H, line width at half height = 15 Hz), 2.84 (m, 1 H, line width at half height = 12 Hz), 2.28 (m, 1 H), 1.35-1.90 (m, 7 H); ¹³C NMR (CDCl₃): δ 164.8, 146.1, 131.8, 130.3, 128.4, 127.3, 126.4, 124.5, 122.0, 89.1, 55.3, 41.8, 39.4, 26.4, 25.2, 24.1, 23.9; IR (neat): 2933, 1634 cm⁻¹; MS: (m/e) 266 (M⁺+1, 18), 265 (M⁺, 99), 264 (27), 263 (M⁺-H₂, 100), 248 (40), 236 (27), 234 (27), 222 (35), 210 (99), 192 (36), 180 (16), 166 (29); HRMS: Calcd. For C₁₈H₁₉NO is 265.146664, found 265.145504. The cis stereochemistry was assigned based on the relatively narrow line widths for the ring junction protons at δ 3.45 and δ 2.84. In the trans isomer, these protons would be axial and would couple to two other axial protons, and should feature much wider and discernable patterns.

Coupling of Carbene Complex **4e** with 2-ethynylbenzaldehyde (**2d**) (Entry E):

General Procedure 4 was followed using carbene complex **4e** (0.355 g, 1.0 mmol) and 2-ethynylbenzaldehyde (**2d**) (0.116 g, 0.89 mmol); in this experiment triphenylphosphine (0.262 g, 1.0 mmol) and toluene was used as the solvent (in place of dioxane). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (1:1) as eluent to yield product **11e** (0.095 g, 42%). ¹H NMR (CDCl₃): δ 9.16 (s, 1 H), 7.10 (d, 1 H, J = 7.7 Hz), 7.70-7.85 (m, 2 H), 7.61 (m, 1 H), 4.02 (d, 1 H, J = 21.8 Hz), 3.76 (d, 1 H, J = 21.8 Hz), 3.49(ddd, 1 H, J = 10.7, 5.0, 3.8 Hz), 3.06 (br s, 1 H, line width at half height = 10 Hz), 2.44 (m, 1 H), 2.07 (m, 1 H), 1.79 (m, 1 H), 1.40-1.70 (m, 4 H), 1.25 (m, 1 H); ¹³C NMR (CDCl₃): δ 209.4, 152.6, 151.4, 134.7, 131.0, 128.5, 127.1, 126.8, 121.8, 120.4, 48.1, 45.8, 38.7, 31.8, 26.0, 24.4, 22.0; IR (neat): 2933, 1713, 1623 cm⁻¹; MS: (m/e) 252 (M⁺+1, 23), 251 (M⁺, 100), 234 (5), 222 (38), 208 (15), 196 (97), 180 (49), 167 (41), 152 (15), 115 (19); HRMS: Calcd. For C₁₇H₁₇NO is 251.131014, found 251.130288. The cis stereochemistry was assigned based on the appearance the

ring junction protons at δ 3.49 (ddd, J = 10.7, 5.0, 3.8 Hz), and δ 3.06 (br s, line width at half height = 10 Hz). In the trans isomer, these protons would be axial and would couple to two other axial protons, and should feature much wider and discernable patterns. The pattern at δ 3.49 is consistent with an axial proton coupled to one other axial proton and two equatorial protons, as expected in the cis isomer. The pattern at δ 3.06 is consistent with contribution from multiple small couplings, as expected for an equatorial proton.

Coupling of Carbene Complex 4d with 1-(2-hex-1-ynyl-phenyl)-ethanone (2b)

(Entry F): General Procedure 4 was followed using carbene complex **4d** (0.10 g, 0.29 mmol) and 1-(2-hex-1-ynyl-phenyl)-ethanone (**2b**) (0.052 g, 0.26 mmol). The crude product was purified using flash chromatography over silica gel with hexane-ethyl acetate (1:1) as eluent to yield product **7f** (0.035 g, 40%). ^1H NMR (CDCl_3): δ 8.07 (d, 2 H, J = 8.0 Hz), 7.40-7.60 (m, 2 H), 3.75 (s, 3 H), 3.20 (m, 1 H), 2.93 (s, 3 H), 2.55-2.92 (m, 3 H), 1.10-1.60 (m, 12 H), 0.77 (t, 3 H, J = 7.0 Hz); ^{13}C NMR (CDCl_3): δ 159.4, 154.3, 149.6, 133.1, 128.6, 128.1, 126.3, 125.9, 125.2, 125.1, 116.5, 57.6, 41.8, 36.4, 31.0, 28.2, 26.3, 25.8, 24.8, 22.8, 22.7, 22.3, 13.8; IR(neat): 2930, 1627 cm^{-1} ; MS: (m/e) 337 (M^++2 , 2), 336 (M^++1 , 26), 335 (M^+ , 100), 320 (M^+-Me , 31), 306 (M^+-Et , 9), 292 (35), 280 (22), 262 (10), 224 (10), 145 (15); HRMS: Calcd. For $\text{C}_{23}\text{H}_{29}\text{NO}$ is 335.224.915, found 335.225687.

Coupling of Carbene Complex 6b with 2-hex-1-ynyl-benzaldehyde (2a) (Entry G):

General Procedure 4 was followed using carbene complex **6a** (0.385 g, 1.10 mmol) and 2-hex-1-ynyl-benzaldehyde (**2a**) (0.186 g, 1.0 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (9:1) as eluent to yield product **13g** (0.130 g, 40%). ^1H NMR (CDCl_3): δ 9.61 (overlapping s and d, J = 8.0 Hz), 8.84 (d, 1 H, J = 8.5 Hz), 8.21 (t, 2 H, J = 7.7 Hz), 8.00 (t, 1 H, J = 7.4 Hz), 7.82 (m, 3 H), 4.00 (s, 3 H), 3.51 (t, 2 H, J = 8.1), 1.88 (m, 2 H), 1.62 (sextet, 2 H, J = 7.3 Hz), 1.03 (t, 3 H, J = 7.3 Hz); ^{13}C NMR (CDCl_3): δ 154.7, 150.1, 133.7, 130.5, 129.3, 127.8, 127.6, 127.3, 126.8, 126.1, 125.3, 121.9, 61.8, 31.7, 28.7, 23.0, 13.7; IR (cm^{-1}): 1615 (m), 1590 (m), 1519 (m), 146 (m) cm^{-1} ; MS: (m/e) 315 (M^+ , 70), 272 ($\text{M}^+-\text{C}_3\text{H}_7$, 100), 229 (29), 185 (19), 316 (21); HRMS: Calcd. For $\text{C}_{22}\text{H}_{21}\text{NO}$ is 315.16232, found 315.16012.

Coupling of Carbene Complex 6b with 2-hex-1-ynyl-benzaldehyde (2a) (Entry H):

General Procedure 4 was followed using carbene complex **6b** (0.385 g, 1.10 mmol) and 2-hex-1-ynyl-benzaldehyde (**2a**) (0.186 g, 1.0 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (9:1) as eluent to yield product **13h** (0.130 g, 40%). ^1H NMR (CDCl_3): δ 9.44 (m, 1 H), 9.38 (s, 1 H), 8.79 (d, 1 H, J = 8.4 Hz), 8.03-8.20 (m, 2 H), 7.60-7.84 (m, 4 H), 3.53 (t, 2 H, J = 7.8 Hz), 3.19 (s, 6 H), 1.55-1.75 (m, 2 H), 1.25-1.50 (m, 2 H), 0.91 (t, 3 H, J = 7.0 Hz); ^{13}C NMR (CDCl_3): δ 151.0, 147.9, 141.2, 135.1, 133.6, 132.5, 132.3, 129.4, 128.6, 127.7, 127.1, 126.4, 126.3, 125.9, 125.7, 124.3, 122.6, 44.3 (2C), 32.1 (2C), 23.1, 13.9; IR (neat): 2915, 1940, 1615, 1379 cm^{-1} ; MS: (m/e) 330 (M^++2 , 4), 329 (M^++1 , 26), 328 (M^+ , 86), 313 (M^+-CH_3 ,

8), 286 (22), 285 (100), 271 (85), 269 (53), 254 (10), 241 (16), 215 (6), 142 (13); HRMS: Calcd. For $C_{23}H_{24}N_2$ is 328.193949, found 328.193884.

Coupling of Carbene Complex **6b with (2-hex-1-ynyl-phenyl)-phenylmethanone (**2c**) (Entry I):** General Procedure 4 was followed using carbene complex **6b** (0.088 g, 0.25 mmol) and (2-hex-1-ynyl-phenyl)-phenyl methanone (**2c**) (0.055 g, 0.21 mmol). The crude product was purified using flash chromatography on silica gel with hexane-ethyl acetate (3:1) as eluent to yield product **13i** (0.051 g, 60%). 1H NMR ($CDCl_3$): δ 9.50 (m, 1 H), 8.82 (d, 1 H, J = 8.0 Hz), 8.29 (d, 1 H, J = 8.0 Hz), 8.16 (m, 1 H), 8.02 (d, 1 H, J = 8.0 Hz), 7.50-7.85 (m, 8 H), 3.56 (t, 2 H, J = 7.5 Hz), 3.23 (s, 6 H), 1.55-1.80 (m, 2 H), 1.25-1.50 (m, 2 H), 0.93 (t, 3 H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$): δ 157.9, 148.0, 140.2, 140.0, 134.8, 133.9, 132.6, 132.4, 130.4 (2C), 128.6, 128.5, 128.2 (3C), 127.0, 126.7, 126.0, 125.9, 125.8, 125.7, 124.3, 122.1, 44.4 (2C), 32.4, 32.2, 23.2, 13.9; IR (neat): 2957, 1940, 1574, 1377 cm^{-1} ; MS: (m/e) 406 ($M^+ + 2$, 3), 405 ($M^+ + 1$, 24), 404 (M^+ , 80), 389 ($M^+ - Me$, 7), 361 (94), 347 (100), 331 (18), 316 (9), 172 (21); HRMS: Calcd. For $C_{29}H_{28}N_2$ is 404.225249, found 404.226090.

Computational Details. The following series of steps were utilized to compute the reaction energies. Each of the species in Scheme 4 was drawn in CHEM 3D and then minimized using MM2. A Gaussian input file was constructed from the MM2 energy-minimized structure. The structure was again minimized using Gaussian 98W⁷ at the B3LYP level using the 6-31G* basis set, followed by a frequency calculation also at the B3LYP level using the 6-31G* basis set. The frequency calculation was conducted using Gaussian 98W at the B3LYP level using the 6-31G basis set. The total thermal energy and entropy were obtained for each species at 298 K; ΔH and ΔS were obtained through addition/subtraction of appropriate numbers based on the interconversions of interest. Free energy was calculated from the equation $\Delta G = \Delta H - T\Delta S$. Values obtained are listed below.

⁷ Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Zakrzewski, V.G.; Montgomery, J.A.; Stratmann, R.E.; Burant, J.C.; Dapprich, S.; Millam, J.M.; Daniels, A.D.; Kudin, K.N.; Strain, M.C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G.A.; Ayala, P.Y.; Cui, Q.; Morokuma, K.; Malick, D.K.; Rabuck, A.D.; Raghavachari, K.; Foresman, J.B.; Cioslowki, J.; Ortiz, J.V.; Stefanov, B.B.; Liu, A.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R.L.; Fox, D.J.; Keith, T.; Al-Laham, M.A.; Peng, C.Y.; Nanayakkara, A.; Gonzalez, M.; Callacombe, M.; Gill, P.M.W.; Johnson, B.G.; Chen, W.; Wong, M.W.; Andres, J.L.; Head-Gordon, M.; Replogle, E.S.; Pople, J.A., Gaussian, Inc., Pittsburgh, PA, 1998.

| <u>SPECIES</u> | <u>THERMAL ENERGY (kcal/mol)</u> | <u>ENTROPY (cal/molK)</u> |
|---------------------|----------------------------------|-----------------------------------|
| A | 95.896 | 87.646 |
| B | 68.639 | 75.512 |
| C | 167.372 | 113.045 |
| D | 152.960 | 118.941 |
| E | 153.760 | 100.289 |
| F | 137.885 | 114.849 |
| G | 138.400 | 99.236 |
| H | 135.315 | 97.607 |
| CO ₂ | 8.935 | 51.165 |
| Cr(CO) ₆ | 40.544 | 120.736 |
| Cr(CO) ₅ | 33.561 | 110.945 (Octahedral minus one CO) |
| | 32.649 | 108.649 (Trigonal bipyramidal) |