

Terms & Conditions

Electronic Supporting Information files are available without a subscription to ACS Web Editions. The American Chemical Society holds a copyright ownership interest in any copyrightable Supporting Information. Files available from the ACS website may be downloaded for personal use only. Users are not otherwise permitted to reproduce, republish, redistribute, or sell any Supporting Information from the ACS website, either in whole or in part, in either machine-readable form or any other form without permission from the American Chemical Society. For permission to reproduce, republish and redistribute this material, requesters must process their own requests via the RightsLink permission system. Information about how to use the RightsLink permission system can be found at <http://pubs.acs.org/page/copyright/permissions.html>



Supplementary Material for

Macrocyclization of Fischer Carbene Complexes as an Approach to Cyclophanes

Huan Wang and William D. Wulff*

Department of Chemistry
Searle Chemistry Laboratory
The University of Chicago
Chicago, Illinois 60637

All reagents were purchased from Aldrich and used without further purification unless otherwise indicated. Tetrahydrofuran and ether were distilled from benzophenone ketyl under nitrogen. Acetonitrile and methylene chloride were distilled from CaH_2 under nitrogen. Benzene was distilled from Na under nitrogen. Chromatographic purifications were performed on Merck silica gel (grade 60, 230 - 400 mesh), and TLC's were performed on Whatman Inc. TLC plates (K6F silica gel 60 Å, thickness 250 μm). ^1H NMR data were obtained either on a Bruker DRX 400 MHz or a Bruker DRX 500 MHz instrument. ^{13}C NMR data were obtained on the same instruments at 100 and 125 MHz, respectively. Infrared spectra were recorded on a Nicolet 20SX FTIR. Mass spectra were obtained from Mass Spectrometry Laboratory of University of Illinois at Urbana-Champaign. Elemental analyses were performed by Galbraith Laboratories in Knoxville, TN. All melting points were measured on a Thomas Unimelt and are uncorrected.

Preparation of 8-nonyl-1-ol 23b.

A potassium hydride dispersion in mineral oil was washed with pentane (10 mL \times 5), and the solvent was removed on high vacuum to give KH powder (1.92 g, 47.83 mmol). Diaminopropane (20 mL, freshly distilled from calcium hydride) was added at 0 °C, and the mixture was stirred at R. T. for one hour, during which time the mixture turned slightly yellow then greenish blue and finally to a yellow suspension. 3-Nonyl-1-ol (from Lancaster, 1.00 mL, 6.22 mmol) was added at R. T., and the resultant red suspension was stirred at R. T. for one hour. Water was slowly added to quench the reaction. The resultant yellow mixture was extracted with ether (25 mL \times 3) and the combined organic layer was washed with HCl (2 N, 25 mL \times 3), brine and then dried with MgSO_4 . The solvent was removed and flash column chromatography on

silica gel yielded the title compound as a colorless oil (827.6 mg, 5.90 mmol, 95%).¹ R_f (ether/hexanes 1/2) 0.18; ¹H NMR (CDCl₃) δ 1.3-1.5 (m, 10H), 1.73 (s, 1H), 1.92 (t, 1H, J = 2.6 Hz), 2.15 (td, 2H, J = 7.0, 2.6 Hz), 3.60 (t, 2H, J = 6.6 Hz); ¹³C NMR (CDCl₃) δ 18.28, 25.53, 28.30, 28.58, 28.80, 32.60, 62.80, 68.08, 84.60; IR (neat) 3294 s, br, 2117 w cm⁻¹. Anal Calcd for C₉H₁₆O: C, 77.09; H, 11.50. Found: C, 76.38; H, 11.37. Alcohols **23d** and **23e** were prepared in the same manner.

12-Tridecyn-1-ol **23d**.

The title compound^{1a} was obtained as a white solid in 91 % yield from 3-tridecyn-1-ol (from Lancaster). R_f (ether/hexanes 1/2) 0.20; ¹H NMR (CDCl₃) δ 1.2-1.3 (m, 14H), 1.53 (m, 5H), 1.92 (t, 1H, J = 2.6 Hz), 2.16 (td, 2H, J = 7.1, 2.7 Hz), 3.61 (t, 2H, J = 6.6 Hz); ¹³C NMR (CDCl₃) δ 18.35, 25.70, 28.45, 28.71, 29.05, 29.38, 29.43, 29.47, 29.53, 32.75, 62.98, 68.01, 84.75; IR (thin film) 3375 br, 3282 s, 2110 w cm⁻¹. Anal Calcd for C₁₃H₂₄O: C, 79.53; H, 12.32. Found: C, 79.66; H, 12.61.

15-Hexadecyn-1-ol **23e**

The title compound^{1b} was obtained as a white solid in 90% yield from 7-hexadecyn-1-ol (from Lancaster) following the procedure for 8-nonyl-1-ol **23b**. R_f (ether/hexanes 1/2) 0.26; ¹H NMR (CDCl₃) δ 1.2-1.4 (m, 21H), 1.54 (m, 4H), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (td, 2H, J = 7.1, 2.6 Hz), 3.64 (t, 2H, J = 6.6 Hz); ¹³C NMR (CDCl₃) δ 18.22, 25.65, 28.35, 28.61, 28.97, 29.33, 29.36, 29.46, 29.50, 32.58, 62.54, 67.95, 84.50, 3 aliphatic carbons were not located; IR (thin film) 3286 m, 2100 w cm⁻¹; MS (Cl) m / z (% rel. intensity) 238 (M⁺, 2), 237 (7), 221 (6), 137 (14), 123 (31), 109 (62), 95 (100), 81 (85), 69 (58). Anal Calcd for C₁₆H₃₀O: C, 80.60; H, 12.68. Found: C, 80.64; H, 13.03.

Preparation of 8-nonyal **9b**.

To a solution of newly distilled (COCl)₂ (440 μ L, 5.04 mmol) in 10 mL of CH₂Cl₂ at -78 °C was added DMSO (vacuum distilled, 720 μ L, 10.15 mmol) in 3 mL of CH₂Cl₂ over 5 minutes. The resultant solution was stirred for 30 minutes at -78 °C and 8-nonyl-1-ol **23b** (639.6 mg, 4.56 mmol) in 5 mL of CH₂Cl₂ was added over 5 minutes. The resultant white suspension was stirred

¹ a) Knapp, F. F.; Srivastava, P. C.; Callahan, A. P.; Cunningham, E. B.; Kabalka, G. W.; Sastry, K. A. R. *J. Med. Chem.* 1984, 27, 57. b) Menger, F. M.; Chen, X. Y.; Brochini, S.; Hopkins, H. P.; Hamilton, D. *J. Am. Chem. Soc.* 1993, 115, 6600

at -78 °C for an additional one hour and Et₃N (distilled over CaH₂, 3.2 mL, 23 mmol) was added. The reaction was stirred at -78 °C for one hour and warmed up to R. T. over another one hour. Water was added to the reaction and the mixture was extracted with CH₂Cl₂ (25 mL × 3). The combined organic layer was washed with HCl (2 N, 25 mL × 2) and brine (25 mL × 2), then dried with MgSO₄. Flash column chromatography on silica gel yielded the title compound as a colorless oil (595.7 mg, 4.32 mmol, 95%). R_f (ether/hexanes 1/4) 0.39; ¹H NMR (CDCl₃) δ 1.34 (m, 2H), 1.41 (m, 2H), 1.51 (m, 2H), 1.62 (m, 2H), 1.92 (t, 1H, J = 2.6 Hz), 2.16 (td, 2H, J = 7.0, 2.6 Hz), 2.41 (td, 2H, J = 7.3, 1.7 Hz), 9.74 (t, 1H, J = 1.8 Hz); ¹³C NMR (CDCl₃) δ 18.23, 21.84, 28.11, 28.32, 28.53, 43.73, 68.22, 84.36, 202.55; IR (neat) 3292 s, 2860 s, 2724 m, 2117 w, 1725 s cm⁻¹; MS (Cl) m / z (% rel. intensity) 137 (M⁺-1, 4), 121 (32), 109 (12), 95 (100), 94 (10), 81 (37), 67 (27). Aldehydes **9c**, **9d** and **9e** were prepared in the same manner.

10-Undecynal **9c**.

The title compound^{2a} was obtained as a colorless oil in 95% yield from 10-undecyn-1-ol (from Lancaster). R_f (ether/hexanes 1/4) 0.46; ¹H NMR (CDCl₃) δ 1.3-1.4 (m, 8H), 1.52 (m, 2H), 1.63 (m, 2H), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (td, 2H, J = 7.0, 2.6 Hz), 2.42 (td, 2H, J = 7.4, 1.8 Hz), 9.76 (t, 1H, J = 1.8 Hz); ¹³C NMR (CDCl₃) δ 17.99, 21.67, 28.07, 28.27, 28.53, 28.73, 28.87, 43.48, 67.94, 84.13, 202.14; IR (neat) 3294 m, 2857 s, 2716 m, 2117 w, 1726 s cm⁻¹; MS (EI) m / z (% rel. intensity) 165 (M⁺-1, 2), 149 (10), 133 (15), 123 (26), 107 (44), 95 (49), 81 (100), 67 (58).

12-Tridecynal **9d**.

The title compound was obtained as a colorless oil in 90% yield from 12-tridecyn-1-ol **23d** following the procedure for 8-nonynal **9b**. R_f (ether/hexanes 1/4) 0.48; ¹H NMR (CDCl₃) δ 1.2-1.4 (m, 12H), 1.52 (m, 2H, J = 7.4 Hz), 1.62 (m, 2H, J = 7.2 Hz), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (td, 2H, J = 7.1, 2.6 Hz), 2.42 (td, 2H, J = 7.4, 1.8 Hz), 9.76 (t, 1H, J = 1.8 Hz); ¹³C NMR (CDCl₃) δ 18.33, 22.02, 28.41, 28.66, 29.00, 29.09, 29.26, 29.28, 29.34, 43.85, 68.02, 84.68, 202.78; IR (neat) 3294 s, 2861 s, 2721 m, 2118 w, 1728 s cm⁻¹; MS (Cl) m / z (% rel. intensity) 194 (M⁺, 4), 193 (9), 177 (28), 176 (2), 151 (5), 121 (32), 109 (51), 95 (100), 81 (74).

15-Hexadecynal **9e**.

² a) Vinczer, P.; Baán, G.; Juvancz, Z.; Novák, L.; Szántay, C. *Syn. Comm.* 1985, 15, 1257. b) Adams, T. C.; Dupont, A. C.; Carter, J. P.; Kachur, J. F.; Guzewska, M. E.; Rzeszotarski, W. J.; Farmer, S. G.; Noronha-Blob, L.; kaiser, C. J. *Med. Chem.* 1991, 34, 1585

The title compound was obtained as a white solid in 84% yield from 15-hexadecyn-1-ol

23e. R_f (ether/hexanes 1/4) 0.48; ^1H NMR (CDCl_3) δ 1.2-1.3 (m, 18H), 1.52 (m, 2H), 1.63 (m, 2H), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (td, 2H, J = 7.1, 2.7 Hz), 2.42 (td, 2H, J = 7.3, 1.8 Hz), 9.76 (t, 1H, J = 1.8 Hz); ^{13}C NMR (CDCl_3) δ 18.28, 21.97, 28.39, 28.65, 29.00, 29.05, 29.25, 29.31, 29.38, 29.45, 29.47, 43.79, 67.96, 84.58, 202.67, 1 aliphatic carbon was not located; IR (thin film) 3244 m, 2847 s, 2746 m, 2115 vw, 1707 s cm^{-1} ; MS (EI) m / z (% rel. intensity) 236 (M^+ , 1), 207 (1), 109 (16), 95 (35), 81 (58), 67 (93), 55 (100).

Preparation of pentacarbonyl (5-hexyn-*trans*-1-enyl)methoxycarbene chromium(0) (10a).

Pentacarbonyl methylmethoxycarbene chromium(0)³ (389.9 mg, 1.56 mmol) was dissolved in 45 mL of ether at -78 °C, and 1 eq. of BuLi was added. The mixture was stirred at -78 °C for 30 min. In a separate flask, freshly distilled SnCl_4 (360 μL , 3.08 mmol) was added to 5-hexynal^{2b} (253.2 mg, 3.09 mmol) in 15 mL of CH_2Cl_2 at -78 °C and the mixture was stirred at -78 °C for 30 min before the anion of the carbene complex was added *via* cannula. The reaction mixture was stirred at -78 °C for 2 hours and quenched by pouring into 50 mL of water. The organic layer was washed with brine and dried. The solvent was removed and the aldol adduct was separated from the unreacted starting carbene complex by column chromatography. The aldol adduct was obtained as a yellow oil (405.5 mg, 1.22 mmol). It was then dissolved in 50 mL of CH_2Cl_2 , and MsCl (vacuum distilled, 195 μL , 2.52 mmol) and Et_3N (distilled over CaH_2 , 390 μL , 2.80 mmol) were added at 0 °C. TLC showed the reaction was completed in 5 min. Saturated NaHCO_3 was added and the mixture was extracted by ether (20 mL \times 3). The combined organic layer was washed with aqueous NaHCO_3 and brine, then dried with MgSO_4 . Flash column chromatography yielded the title compound as a red oil (203.7 mg, 0.653 mmol, 42%). R_f (hexanes) 0.16; ^1H NMR (CDCl_3) δ 2.02 (t, 1H, J = 2.2 Hz), 2.40 (m, 4H), 4.76 (s, 3H), 6.27 (m, 1H), 7.38 (d, 1H, J = 15 Hz); ^{13}C NMR (CDCl_3) δ 17.60, 30.98, 66.49, 69.69, 82.46, 132.70, 144.83, 216.57, 223.96, 336.44; IR (neat) 3311 m, 2142 vw, 2060 s, 1924 vs, 1608 m cm^{-1} ; MS (EI) m / z (% rel. intensity) 314 (M^+ , 10), 286 (1), 258 (18), 230 (37), 202 (87), 174 (100), 159 (87), 142 (70), 122 (13). Carbene complexes **10b**, **10c**, **10d** and **10e** were prepared in the same manner:

³ Hegedus, L. S.; McGuire, M. A.; Schultze, L. M. *Org. Synth.* **1993**, Coll. Vol. VIII, 216.

Pentacarbonyl (9-decyn-*trans*-1-enyl)methoxycarbene chromium(0) 10b.

The title compound was obtained as a red oil in 57% yield from 8-nonynal **9b**. R_f (hexanes) 0.14; ^1H NMR (CDCl_3) δ 1.3-1.6 (m, 8H), 1.94 (t, 1H, J = 2.5 Hz), 2.19 (m, 4H), 4.74 (s, 3H), 6.31 (m, 1H), 7.29 (d, 1H, J = 15 Hz); ^{13}C NMR (CDCl_3) δ 18.42, 28.20, 28.34, 28.50, 28.73, 32.34, 66.33, 68.19, 84.47, 137.03, 144.20, 216.38, 223.55, 335.17; IR (neat) 3313 m, 2123 vw, 2059 s, 1985 s, shoulder, 1931 vs cm^{-1} ; MS (EI) m / z (% rel. intensity) 370 (M^+ , 10), 314 (14), 286 (2), 258 (11), 230 (74), 226 (100), 178 (16). Anal Calcd for $\text{C}_{17}\text{H}_{18}\text{O}_6\text{Cr}$: C, 55.14; H, 4.90. Found: C, 54.73; H, 5.17.

Pentacarbonyl (11-dodecyn-*trans*-1-enyl)methoxycarbene chromium(0) 10c.

The title compound was obtained as a red oil in 48% yield from 10-undecynal **9c**. R_f (hexanes) 0.17; ^1H NMR (CDCl_3) δ 1.3-1.5 (m, 12H), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (m, 4H), 4.73 (s, 3H), 6.32 (dt, 1H, J = 15, 7.2 Hz), 7.28 (d, 1H, J = 15 Hz); ^{13}C NMR (CDCl_3) δ 18.30, 28.20, 28.37, 28.60, 28.88, 29.08, 29.16, 32.31, 66.26, 68.04, 84.61, 137.53, 144.34, 216.74, 223.91, 335.89; IR (neat) 3311 w, 2115 vw, 2059 s, 1983 m, shoulder, 1928 vs cm^{-1} ; MS (Cl) m / z (% rel. intensity) 398 (M^+ , 13), 370 (6), 342 (32), 315 (24), 314 (17), 286 (42), 259 (100), 258 (45), 235 (91), 207 (43), 137 (100).

Pentacarbonyl (13-tetradecyn-*trans*-1-enyl)methoxycarbene chromium(0) 10d.

The title compound was obtained as a red oil in 60% yield from 12-tridecynal **9d**. R_f (hexanes) 0.10; ^1H NMR (CDCl_3) δ 1.2-1.5 (m, 16H), 1.94 (t, 1H, J = 2.7 Hz), 2.18 (m, 4H), 4.73 (s, 3H), 6.33 (dt, 1H, J = 15, 7.2 Hz), 7.28 (d, 1H, J = 15 Hz); ^{13}C NMR (CDCl_3) δ 18.38, 28.28, 28.47, 28.72, 29.06, 29.20, 29.35, 29.42, 32.39, 66.32, 68.03, 84.77, 137.64, 144.37, 216.79, 223.96, 335.94, 1 aliphatic carbon was not located; IR (neat) 3312 m, 2160 vw, 2059 s, 1986 s, shoulder, 1939 vs cm^{-1} ; MS (EI) m / z (% rel. intensity) 426 (M^+ , 1), 370 (1), 314 (1), 286 (3), 264 (6), 262 (66), 71 (64), 57 (100).

Pentacarbonyl (16-heptadecyn-*trans*-1-enyl)methoxycarbene chromium(0) 10e.

The title compound was obtained as a red oil in 33% yield from 15-hexadecynal **9e**. R_f (hexanes) 0.18; ^1H NMR (CDCl_3) δ 1.2-1.5 (m, 22H), 1.94 (t, 1H, J = 2.6 Hz), 2.18 (m, 4H), 4.73 (s, 3H), 6.33 (dt, 1H, J = 15, 7.2 Hz), 7.28 (d, 1H, J = 15 Hz); ^{13}C NMR (CDCl_3) δ 18.38, 28.28, 28.48,

28.74, 29.08, 29.21, 29.37, 29.47, 29.57, 29.68, 32.39, 66.29, 68.00, 84.77, 137.68, 144.35, 216.77, 223.95, 335.97, 2 aliphatic carbons were not located; IR (neat) 3313 w, 2118 vw, 2059 s, 1983 m, shoulder, 1928 vs cm^{-1} ; MS (Cl) m / z (% rel. intensity) 468 (M^+ , 3), 440 (2), 412 (4), 385 (3), 357 (13), 356 (6), 329 (33), 328 (22), 305 (100), 277 (21), 221 (30), 193 (38).

General procedure for benzannulation reaction of carbene complexes 10a-10e.

The carbene complex was dissolved in the solvent and at the concentration indicated in Table I, deoxygenated by freeze-pump-thaw method (3 cycles), and heated in an oil bath to the temperature indicated in Table 1. The solution turned from red to yellow during the reaction. The reaction time was 14-18 hours at 60 °C or 0.2-4 hours at 100 °C. After the completion of the reaction, the yellow solution was stirred in air overnight, concentrated on a rotavap and then chromatographed to give the products indicated in Table I.

12,24-Dihydroxy-9,21-dimethoxy-[6,6]-metacyclophane 12b.

White solid. R_f (ether/CH₂Cl₂/hexanes 1/1/4) 0.46; mp 119-120 °C (recrystallized from ether/pentane); ¹H NMR (CDCl₃) δ 1.5-1.6 (m, 16H), 2.56 (t, 8H, J = 7.8 Hz), 3.74 (s, 6H), 4.59 (s, 2H), 6.53 (s, 4H); ¹³C NMR (CDCl₃) δ 27.04, 28.87, 30.05, 55.54, 113.08, 130.45, 145.02, 153.21; IR (thin film) 3261 s, br, 1213 m, 847 w cm^{-1} ; MS (EI) m / z (% rel. intensity) 412 (M^+ , 100), 151 (33), 137 (21), 121 (15), 91 (19), 77 (12); Anal Calcd for C₂₆H₃₆O₄: C, 75.69; H, 8.79. Found: C, 75.56; H, 9.21.

12,24,36-Trihydroxy-9,21,33-trimethoxy-[6,6,6]-metacyclophane 13b.

Pale yellow oil. R_f (ether/CH₂Cl₂/hexanes 1/1/2) 0.50; ¹H NMR (CDCl₃) δ 1.36 (m, 12H), 1.59 (m, 12H), 2.52 (t, 12H, J = 7.4 Hz), 3.73 (s, 9H), 4.24 (s, 3H), 6.50 (s, 6H); ¹³C NMR (CDCl₃) δ 28.81, 29.37, 30.43, 55.58, 112.98, 129.20, 145.40, 153.03; IR (neat) 3477 br, 1194 s cm^{-1} ; MS (EI) m / z (% rel. intensity) 618 (M^+ , 100), 440 (32), 412 (74), 396 (51), 151 (82). Anal Calcd for C₃₉H₅₄O₆: C, 75.69; H, 8.79. Found: C, 75.24; H, 9.08.

14-Hydroxy-11-methoxy-[8]-metacyclophane 11c⁴:

Pale yellow oil. R_f (ether/CH₂Cl₂/hexanes 1/1/10) 0.31; ¹H NMR (CDCl₃) δ 0.16 (m, 2H), 0.8-1.6 (m, 8H), 2.03 (m, 2H), 2.45 (m, 2H), 2.90 (m, 2H) 3.75 (s, 3H), 4.49 (s, 1H), 6.46 (s, 2H); IR (neat) 3463 br, 1184 s cm⁻¹; MS (EI) m / z (% rel. intensity) 234 (M⁺, 100), 191 (5), 150 (16), 137 (12); m / z calcd for C₁₅H₂₂O₂: 234.1620, found: 234.1623.

14,28-Dihydroxy-11,25-dimethoxy-[8,8]-metacyclophane 12c.

White solid, mp 104-106 °C; R_f (ether/CH₂Cl₂/hexanes 1/1/4) 0.49; ¹H NMR (CDCl₃) δ 1.34 (m, 16H), 1.60 (m, 8H), 2.56 (t, 8H, J = 7.6 Hz), 3.75 (s, 6H), 4.44 (s, 2H), 6.53 (s, 4H); ¹³C NMR (CDCl₃) δ 27.62, 27.86, 29.14, 30.00, 55.58, 112.96, 129.55, 145.40, 153.14; IR (thin film) 3383 br, 1196 m cm⁻¹; MS (EI) m / z (% rel. intensity) 468 (M⁺, 56), 234 (34), 219 (10), 177 (19), 151 (100).

14,28,42-Trihydroxy-11,25,39-trimethoxy-[8,8,8]-metacyclophane 13c.

Pale yellow oil. R_f (ether/CH₂Cl₂/hexanes 1/1/4) 0.28; ¹H NMR (CDCl₃) δ 1.31 (m, 24H), 1.55 (m, 12H), 2.54 (t, 12H, J = 7.6 Hz), 3.74 (s, 9H), 4.31 (s, 3H), 6.52 (s, 6H); ¹³C NMR (CDCl₃) δ 28.99, 29.04, 29.68, 30.44, 55.62, 112.92, 129.28, 145.42, 153.10; IR (neat) 3474 br, 1194 s cm⁻¹; MS (EI) m / z (% rel. intensity) 702 (M⁺, 66), 496 (8), 468 (51), 454 (46), 447 (29), 366 (41), 234 (32), 55 (100).

16-Hydroxy-13-methoxy-[10]-metacyclophane 11d.

Pale yellow oil. R_f (ether/CH₂Cl₂/hexanes 1/1/10) 0.42; ¹H NMR (CDCl₃) δ 0.69 (m, 2H), 0.93 (m, 4H), 1.19 (m, 2H), 1.31 (m, 4H), 1.45 (m, 2H), 2.01 (m, 2H), 2.47 (m, 2H), 2.90 (m, 2H) 3.76 (s, 3H), 4.47 (s, 1H), 6.54 (s, 2H); ¹³C NMR (CDCl₃) δ 26.45, 26.79, 27.12, 27.44, 30.46, 55.63, 113.66, 129.44, 146.27, 153.44; IR (neat) 3494 br, 1184 s, 757 m cm⁻¹; MS (EI) m / z (% rel. intensity) 262 (M⁺, 100), 219 (1), 151 (13), 137 (13). Anal Calcd for C₁₇H₂₆O₂: C, 77.82; H, 9.99. Found: C, 77.55; H, 10.00.

16,32-Dihydroxy-13,29-dimethoxy-[10,10]-metacyclophane 12d.

R_f (ether/CH₂Cl₂/hexanes 1/1/4) 0.48; ¹H NMR (CDCl₃) δ 1.2-1.3 (m, 24H), 1.5-1.6 (m, 8H), 2.56 (t, 8H, J = 7.6 Hz), 3.74 (s, 6H), 4.30 (s, 2H), 6.53 (s, 4H); ¹³C NMR (CDCl₃) δ 28.67, 28.70,

⁴ This compound appeared to be unstable and no clean ¹³C NMR was obtained.

28.83, 29.68, 30.42, 55.62, 112.97, 129.35, 145.47, 153.05; IR (neat) 3466 br cm^{-1} ; MS (EI) m / z (% rel. intensity) 524 (M^+ , 100), 262 (7), 191 (2), 151 (25), 137 (15).

19-Hydroxy-16-methoxy-[13]-metacyclophane 11e.

Pale yellow oil. R_f (ether/CH₂Cl₂/hexanes 1/1/10) 0.45; R_f (CHCl₃/hexanes 1/1) 0.43; ¹H NMR (CDCl₃) δ 1.0-1.3 (m, 18H), 1.66 (m, 4H), 2.64 (t, 4H, J = 6.2 Hz), 3.75 (s, 3H), 4.29 (s, 1H), 6.52 (s, 2H); ¹³C NMR (CDCl₃) δ 26.17, 26.71, 26.82, 27.15, 27.27, 28.87, 29.65, 55.62, 113.62, 128.69, 145.91, 152.91; IR (neat) 3506 br, 1187 s, 763 m cm^{-1} ; MS (EI) m / z (% rel. intensity) 304 (M^+ , 100), 163 (29), 151 (76), 137 (80), 121 (35), 91 (44), 77 (24).

Preparation of *trans, trans*-1,10-diiodo-1,9-decadiene 28.

1,9-Decadiyne (from GFS, 0.610 mL, 3.71 mmol) and catecholborane (1.00 mL, 9.38 mmol) were dissolved in 10 mL of THF and heated to reflux for 16 hours. The reaction mixture was then cooled to R. T. and the solvent was removed. Water (10 mL) was added and the resultant suspension was stirred at R. T. for 2 hours. The mixture was cooled to 0 °C and the white precipitate was collected by filtration and washed with iced water. The solid was taken up in 10 mL of ether and 11 mL of NaOH (2 N) was added followed by I₂ (2.26 g, 8.92 mmol) in 15 mL of ether at 0 °C. The mixture was stirred at 0 °C for 30 minutes, quenched with satd. Na₂S₂O₃, then extracted with ether. The combined organic layer was washed with Na₂S₂O₃, brine, and dried with MgSO₄. The solvent was removed and flash column chromatography yielded the title compound as a yellow oil (856.0 mg, 2.19 mmol, 59%). R_f (hexanes) 0.61; ¹H NMR (CDCl₃) δ 1.28 (m, 4H), 1.38 (t, 4H, J = 7.0 Hz), 2.04 (qd, 4H, J = 7.2, 1.4 Hz), 5.97 (dt, 2H, J = 14.0, 1.4 Hz), 6.50 (dt, 2H, J = 14.0, 7.2 Hz); ¹³C NMR δ 28.18, 28.58, 35.94, 74.43, 146.55; IR (neat) 3046 m, 1605 m, 944 cm^{-1} .

Preparation of *trans, trans*-1,10-di-[pentacarbonylchromium(0) methoxy carbonyl]-1,9-decadiene 15.

trans, trans-1,10-Diiodo-1,9-decadiene 28 (647.4 mg, 1.66 mmol) was dissolved in 15 mL of THF and *t*-BuLi (6.68 mmol) was added at -78 °C. The resultant yellow gel was stirred at -78 °C for 1.5 hours and Cr(CO)₆ (1039.5 mg, 4.72 mmol) in 35 mL of THF was added. The mixture was then stirred at R. T. for 3 hours and the solvent was removed on rotavap. The red residue was taken up in 15 mL of H₂O and methyl Meerwein's salt (508.2 mg, 3.44 mmol) was added. The mixture turned red and was stirred at R. T. for 15 minutes before being quenched by

NaHCO_3 . Usual workup and flash column chromatography yielded the title compound as a red solid (77.3 mg, 0.128 mmol, 8%). R_f (hexanes) 0.08; ^1H NMR (CDCl_3) δ 1.3-1.5 (m, 8H), 2.17 (m, 4H), 4.74 (s, 6H), 6.30 (dt, 2H, J = 15, 7 Hz), 7.28 (d, 2H, J = 15 Hz).

Benzannulation of *bis*-carbene complex 15 and 1,9-decadiyne.

The *bis*-carbene complex 15 (77.3 mg, 0.128 mmol) was dissolved in 51 mL of THF and 1,9-decadiyne (21 μL , 0.128 mmol) was added. The mixture was deoxygenated by freeze-pump-thaw method (3 cycles) and heated to 100 °C for 30 minutes. TLC showed the reaction was complete. The yellow solution was then stirred in air overnight. The solvent was removed and flash column chromatography yielded 12b (16.3 mg, 0.0396 mmol, 31%).

Preparation of 16-phenyl-15-hexadecyn-1-ol 24.

15-Hexadecyn-1-ol 23e (406.2 mg, 1.70 mmol), bromobenzene (freshly distilled, 360 μL , 3.42 mmol) and $(\text{PPh}_3)_4\text{Pd}$ (394.3 mg, 0.341 mmol) were dissolved in 10 mL of newly distilled pyrrolidine, and the mixture was heated to 80 °C for 3 hours. Aqueous NH_4Cl was added to quench the reaction and the mixture was extracted with ether. The organic layer was dried with MgSO_4 and the solvent was removed. Flash column chromatography yielded the title compound as a white solid (480.6 mg, 1.53 mmol, 90%). Mp 50-51 °C; R_f (ether/hexanes 1/2) 0.21; ^1H NMR (CDCl_3) δ 1.3-1.6 (m, 25H), 2.40 (t, 2H, J = 7.1 Hz), 3.63 (t, 2H, J = 6.6 Hz), 7.2 -7.4 (m, 5H); ^{13}C NMR (CDCl_3) δ 19.38, 25.72, 28.74, 28.90, 29.14, 29.41, 29.51, 29.59, 29.62, 32.78, 63.04, 80.52, 90.45, 124.08, 127.40, 128.13, 131.50, 3 aliphatic carbons were not located; IR (thin film) 3348 m, 754 w, 693 m cm^{-1} ; MS (Cl) m / z (% rel. intensity) 314 (M^+ , 5), 313 (10), 297 (23), 296 (1), 171 (47), 157 (67), 143 (37), 130 (85), 117 (100). Anal Calcd for $\text{C}_{22}\text{H}_{34}\text{O}$: C, 84.02; H, 10.90. Found: C, 83.68; H, 11.18.

Preparation of 16-phenyl-15-hexadecynal 26.

The title compound was obtained as a white solid in 87% yield from 16-phenyl-15-hexadecyn-1-ol 24 following the procedure for 8-nonynal 9b. R_f (ether/hexanes 1/4) 0.48; ^1H NMR (CDCl_3) δ 1.3 (m, 16H), 1.45 (m, 2H), 1.62 (m, 4H), 2.41 (m, 4H), 7.2-7.4 (m, 5H), 9.76 (t, 1H, J = 1.8 Hz); ^{13}C NMR (CDCl_3) δ 19.37, 22.04, 28.73, 28.88, 29.12, 29.31, 29.38, 29.48, 29.53, 29.56, 43.86, 80.52, 90.42, 124.08, 127.39, 128.12, 131.48, 202.86, 2 aliphatic carbons were not located; IR (thin film) 2851 s, 2712 vw, 2239 vw, 1726 s, 755 m, 691 m cm^{-1} ; MS (EI) m / z (% rel. intensity) 312 (M^+ , 8), 284 (2), 171 (9), 157 (21), 143 (39), 130 (100), 117 (57), 91 (28).

Preparation of pentacarbonyl (17-phenyl-16-heptadecyn-*trans*-1-enyl)methoxycarbene chromium(0) 16.

The title compound was obtained as a red oil in 52% yield from 16-phenyl-15-hexadecynal **26** following the procedure for **10a**. R_f (hexanes) 0.11; ^1H NMR (CDCl_3) δ 1.2-1.6 (m, 22H), 2.19 (m, 2H), 2.43 (t, 2H, J = 7.1 Hz), 4.76 (s, 3H), 6.36 (dt, 1H, J = 15, 7.2 Hz), 7.2-7.4 (m, 6H); ^{13}C NMR (CDCl_3) δ 19.37, 28.26, 28.74, 28.89, 29.12, 29.20, 29.36, 29.48, 29.58, 32.37, 66.24, 80.54, 90.41, 124.12, 127.38, 128.11, 131.49, 137.73, 144.32, 216.76, 223.92, 335.90, 3 aliphatic carbons were not located; IR (neat) 2234 vw, 2062 s, 1983 s, shoulder, 1927 vs, 1603 cm^{-1} .

Benzannulation of pentacarbonyl (17-phenyl-16-heptadecyn-*trans*-1-enyl)methoxy-carbene chromium(0) 16.

The carbene complex **16** (136.2 mg, 0.250 mmol) was dissolved in 50 mL of THF, deoxygenated by freeze-pump-thaw method (3 cycles), and heated at 100 °C for 4.5 h. Usual workup and flash column chromatography yielded compound **18** and **21** in 53% and 13% yield, respectively.

15-Phenyl-16-hydroxy-19-methoxy-[13]-paracyclophane 18.

Pale yellow oil. R_f (ether/ CH_2Cl_2 /hexanes 1/1/10) 0.56; ^1H NMR (CDCl_3) δ 1.0-1.3 (m, 19H), 1.47 (m, 1H), 1.62 (m, 1H), 1.76 (m, 1H), 2.22 (m, 1H), 2.32 (m, 1H), 2.83 (m, 1H), 3.06 (m, 1H), 3.82 (s, 3H), 4.34 (s, 1H), 6.70 (s, 1H), 7.2-7.5 (m, 5H); ^{13}C NMR (CDCl_3) δ 26.36, 26.40, 26.64, 27.11, 27.52, 27.57, 27.80, 27.89, 28.07, 28.23, 28.34, 28.37, 30.20, 56.17, 113.24, 125.87, 127.25, 127.92, 128.93, 129.14, 129.38, 130.70, 131.18, 136.04, 144.61, 151.43; IR (neat) 3558 s, 1025 w, 765 m, 705 s cm^{-1} ; MS (EI) m/z (% rel. intensity) 380 (M^+ , 100), 211 (10). Anal Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_2$: C, 82.06; H, 9.53. Found: C, 81.95; H, 9.81.

NOE experiment: irradiation at δ 4.34, observed: 3.1% enhancement at δ 7.33; 1.2% enhancement at δ 6.70.

15-Phenyl-19-hydroxy-16-methoxy-[13]-metacyclophane 21.

Pale yellow oil. R_f (ether/ CH_2Cl_2 /hexanes 1/1/10) 0.42; ^1H NMR (CDCl_3) δ 1.1-1.5 (m, 20H), 1.73 (m, 2H), 2.53 (t, 2H, J = 6.6 Hz), 2.74 (t, 2H, J = 6.3 Hz), 3.65 (s, 3H), 4.43 (s, 1H), 6.62 (s, 1H), 7.2-7.4 (m, 5H); ^{13}C NMR (CDCl_3) δ 26.47, 26.51, 26.54, 26.67, 26.74, 26.82, 27.24,

27.43, 27.59, 28.51, 29.23, 29.83, 56.56, 111.55, 126.55, 127.19, 127.78, 127.89, 130.23, 130.49, 137.86, 146.12, 150.70, 1 aliphatic carbon was not located; IR (neat) 3551 br, 762 m, 702 cm^{-1} ; MS (EI) m / z (% rel. intensity) 380 (M^+ , 100), 225 (14), 55 (10).

NOE experiment: irradiation at δ 4.43, observed: no enhancement at δ 7.2-7.4; no enhancement at δ 6.62; 3.8% enhancement at δ 2.74; 4.7% enhancement at δ 2.53.

Preparation of 16-trimethylsilyl-15-hexadecyn-1-ol 25.

15-Hexadecyn-1-ol **23e** (539.5 mg, 2.26 mmol) was dissolved in 20 mL of THF and 1.80 mL of EtMgBr (3.0 M, 5.4 mmol) was added at R. T. The mixture was stirred at R. T. for 3 h. Freshly distilled TMSCl (0.720 mL, 5.67 mmol) was added to the resultant suspension, and the mixture was stirred overnight. HCl (2 N, 10 mL) was added and the mixture was stirred for 0.5 h at R. T., then extracted with ether. The organic layer was dried with MgSO_4 and the solvent was removed. Flash column chromatography yielded the title compound as a colorless oil (631.0 mg, 2.03 mmol, 90%). R_f (ether/hexanes 1/2) 0.32; ^1H NMR (CDCl_3) δ 0.14 (s, 9H), 1.2-1.5 (m, 25H), 2.21 (t, 2H, J = 7.2 Hz), 3.64 (m, 2H); ^{13}C NMR (CDCl_3) δ 0.01, 19.67, 25.67, 28.47, 28.63, 28.94, 29.35, 29.45, 29.49, 29.51, 32.57, 62.46, 84.02, 107.52, 3 aliphatic carbons were not located; IR (thin film) 3341 s, br, 2176 m cm^{-1} ; MS (Cl) m / z (% rel. intensity) 310 (M^+ , 1), 219 (20), 132 (17), 109 (30), 97 (19), 95 (46), 91 (100), 75 (82).

Preparation of 16-trimethylsilyl-15-hexadecynal 27.

The title compound was obtained as a colorless oil in 81% yield from 16-trimethylsilyl-15-hexadecyn-1-ol **25** following the procedure for 8-nonynal **9b**. R_f (ether/hexanes 1/4) 0.61; ^1H NMR (CDCl_3) δ 0.14 (s, 9H), 1.26 (m, 18H), 1.50 (m, 2H), 1.63 (m, 2H), 2.21 (t, 2H, J = 7.2 Hz), 2.41 (td, 2H, J = 7.4, 1.8 Hz), 9.76 (t, 1H, J = 1.9 Hz); ^{13}C NMR (CDCl_3) δ 0.01, 19.65, 21.91, 28.45, 28.60, 28.90, 29.00, 29.20, 29.26, 29.31, 29.40, 29.43, 43.71, 83.96, 104.77, 202.17, 1 aliphatic carbon was not located; IR (neat) 2852 s, 2714 m, 2174 s, 1728 s cm^{-1} ; MS (EI) m / z (% rel. intensity) 308 (M^+ , 2), 293 (92), 265 (2), 154 (11), 129 (14), 109 (18), 73 (100).

Preparation of pentacarbonyl (17-trimethylsilyl-16-heptadecyn-*trans*-1-enyl)methoxycarbene chromium(0) 17.

The title compound was obtained as a red oil in 48% yield from 16-trimethylsilyl-15-hexadecynal **27** following the procedure for **10a**. R_f (hexanes) 0.21, ^1H NMR (CDCl_3) δ 0.15 (s, 9H), 1.2-1.5 (m, 22H), 2.19 (m, 4H), 4.73 (s, 3H), 6.33 (dt, 1H, J = 15, 7.1 Hz), 7.28 (d, 1H, J = 15

Hz); ^{13}C NMR (CDCl_3) δ 0.15, 19.82, 28.28, 28.61, 28.76, 29.05, 29.22, 29.37, 29.48, 29.58, 32.38, 66.27, 84.19, 107.74, 137.66, 144.36, 216.77, 223.93, 335.97, 3 aliphatic carbons were not located; IR (neat) 2175 m, 2058 s, 1984 s, shoulder, 1952 vs cm^{-1} ; MS (Cl) m / z (% rel. intensity) 540 (M^+ , 1), 475 (12), 447 (57), 309 (36), 293 (35), 219 (12), 73 (100).

Benzannulation of pentacarbonyl (17-trimethylsilyl-16-heptadecyn-*trans*-1-enyl)methoxycarbene chromium(0) 17 and desilylation.

The carbene complex 17 (139.4 mg, 0.258 mmol) was dissolved in 52 mL of THF, deoxygenated by freeze-pump-thaw method (3 cycles), and heated at 100 °C for 5 h. The reaction mixture was then stirred in air overnight. The solvent was removed. The residue was redissolved in 3 mL of CH_2Cl_2 , and stirred with 2 mL of freshly distilled trifluoroacetic acid for 30 min at R. T. Usual workup and flash column chromatography yielded compound 20 and 11e in 12% and 19% yield, respectively.

16-Hydroxy-19-methoxy-[13]-paracyclophane 20.

Pale yellow oil. R_f (ether/ CH_2Cl_2 /hexanes 1/1/10) 0.37; ^1H NMR (CDCl_3) δ 0.9-1.6 (m, 22H), 2.16 (m, 1H), 2.33 (m, 1H), 2.90 (m, 1H), 3.00 (m, 1H), 3.77 (s, 3H), 4.27 (s, 1H), 6.56 (s, 1H), 6.59 (s, 1H); ^{13}C NMR (CDCl_3) δ 26.38, 26.49, 27.02, 27.41, 27.74, 28.12, 28.39, 28.43, 29.43, 29.85, 56.30, 113.79, 117.80, 125.73, 129.80, 146.97, 151.78, 3 aliphatic carbons were not located; IR (neat) 3439 m, br, 1199 s, 845 m cm^{-1} ; MS (EI) m / z (% rel. intensity) 304 (M^+ , 100), 177 (15), 163 (42), 151 (62), 137 (75), 121 (33), 107 (22), 91 (38), 77 (19).