Rh¹-Catalyzed Two-Component [(5+2)+1] Cycloaddition Approach toward [5-8-5] Ring Systems

Feng Huang, Zhong-Ke Yao, Yi Wang, Yuanyuan Wang, Jialing Zhang, and Zhi-Xiang Yu*[^a]

[asian_201000053_sm_misellaneous_information.pdf]
Supporting Information

Rh(I)-Catalyzed Two-Component [(5+2)+1] Cycloaddition Approach toward [5-8-5] Ring Systems

Feng Huang, Zhongke Yao, Yi Wang, Yuanyuan Wang, Jialing Zhang, and Zhi-Xiang Yu*

Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

E-mail: yuzx@pku.edu.cn

Contents

1. General Methods of Synthesis ........................................................................................................... S2
2. General Procedure for the Preparation of Ene-VCP Substrates......................................................... S3
3. General Procedure for the [(5 + 2) + 1] Cycloaddition Reactions ................................................... S12
4. Summary of all [(5 + 2) + 1] Cycloaddition Reactions.................................................................... S13
5. Physical Data for Cycloadducts ........................................................................................................ S15
6. X-Ray Structure for Cycloadducts 11, 17a, 21, and NOESY Correlations...................................... S19
7. Stereochemistry Determination........................................................................................................ S22
8. DFT Calculations and Cartesian Coordinates of Computed Species............................................... S23
9. References.......................................................................................................................................... S26
10. $^1$H and $^{13}$C Spectra for all New Compounds................................................................................ S27
1. General Methods of Synthesis

Air and moisture sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry CO mixed gas or nitrogen from a balloon, unless otherwise indicated. Similarly sensitive liquids and solutions were transferred via syringe. Reactions were stirred using Teflon-coated magnetic stir bars. Elevated temperatures were maintained using thermostat-controlled silicone oil baths. Organic solutions were concentrated using a Büchi rotary evaporator with a desktop vacuum pump. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone prior to use. Dioxane (extra dry, water < 50 ppm), \([\text{Rh(CO)}_2\text{Cl}]_2\) was commercially available and used as received. Analytical TLC was performed with 0.25 mm silica gel 60F plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with acidic \(p\)-anisaldehyde stain followed by gentle heating. Purification of products was accomplished by flash chromatography on silica gel and the purified compounds show a single spot by analytical TLC.

NMR spectra were measured on a Varian INOVA 600 (\(^1\text{H}\) at 600 MHz, \(^{13}\text{C}\) at 150 MHz) magnetic resonance spectrometer. Data for \(^1\text{H}\)-NMR spectra are reported as follows: chemical shift (ppm: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for \(^{13}\text{C}\)-NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak. Infrared spectra were recorded on an AVATAR 330 Fourier transform spectrometer (FT-IR) and are reported in wavenumbers (cm\(^{-1}\)). Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a VG-ZAB-HS mass spectrometer (EI, 70 eV).

Abbreviations:

THF = tetrahydrofuran
PE = petroleum ether
EA = ethyl acetate
DCE = 1,2-dichloroethane
PCC: Pyridinium Chlorochromate
PDC: Pyridinium Dichromate
DIBAL-H: Diisobutylaluminum Hydride
DEAD = diethyl azodicarboxylate
m.p. = melting point
2. General Procedure for the Preparation of Ene-VCP Substrates

(1) Procedure for the Preparation of Bicyclo[3.1.0]hexane-1-carboaldehyde (S4)

\[
\begin{align*}
&\text{Cyclopent-1-enecarboaldehyde (S1)}^{[1]} \\
&\text{To a solution of sodium periodate (20.3 g, 94.8 mmol) in H}_2\text{O (150 mL) at 0 °C was added} \\
&1,2-diol-cyclohexane (10.0 g, 86.2 mmol) dropwise over 10 min. After stirring for 10 min, a solution of \\
&\text{Et}_2\text{O (80 mL) and 2 N NaOH (40 mL) was added consecutively. Then the reaction was stirred for 1 h} \\
&\text{at room temperature. The mixture was extracted with Et}_2\text{O (40 mL x 3). After washing with saturated} \\
&\text{water and brine, the combined organic layer was dried over MgSO}_4\text{ and concentrated. The residue was} \\
&\text{purified by flash column chromatography to afford 4.7 g (62%) S1 as a colorless oil.}
\end{align*}
\]

\[
\begin{align*}
&\text{Cyclopentenylmethanol (S2)}^{[2]} \\
&A \text{ solution of 5.17 g (53.8 mmol) S1 dissolved in 50 mL of methanol was cooled to 0°C. Then NaBH}_4 \\
&\text{(0.6 g, 16 mmol) was added in small portion to the above prepared solution over 10 minutes. After 2 h,} \\
&\text{the reaction solution was evaporated to about one-half volume under reduced pressure. The reaction} \\
&\text{was then quenched with water and the resulting aqueous phase was extracted with ether and washed} \\
&\text{with brine. The combined ether phase was dried over anhydrous Na}_2\text{SO}_4\text{. After removal of the solvent,} \\
&\text{the residue was purified by flash column chromatography to give 4.8 g (91%) S2 as a colorless liquid.}
\end{align*}
\]

\[
\begin{align*}
&\text{Bicyclo[3.1.0]hexane-1-methanol (S3)}^{[3]} \\
&\text{Diethyl zinc solution (19.2 mL, 1.5 M in hexane, 28.8 mmol) and CH}_2\text{I}_2\text{ (4.6 mL, 57.4 mmol) were} \\
&\text{sequentially added to a solution of S2 (2.8 g, 28.7 mmol) in anhydrous CH}_2\text{Cl}_2\text{ (40 mL) at 0 °C. The} \\
&\text{reaction mixture gradually became a white suspension while stirred at 0 °C. The reaction was} \\
&\text{monitored by TLC. After 12 h, the reaction was quenched with saturated NH}_4\text{Cl. The resulting mixture}
\end{align*}
\]
was extracted with ether and the combined organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash column chromatography to afford 2.5 g (80%) S₃ as a colorless oil.

Bicyclo[3.1.0]hexane-1-carboaldehyde (S₄)
SiO₂ (6.9 g) was added to a solution of 1.8 g (16.0 mmol) S₃ in 100 mL of CH₂Cl₂. Two equivalents of PCC (6.9 g, 32.0 mmol) were added dropwise to the above solution over 10 minutes. The resulting mixture was stirred at room temperature for 2 h. Then the reaction mixture was filtered and the precipitate was washed with excess Et₂O. The organic layers were collected and dried over MgSO₄. After concentrated, the residue was purified by flash column chromatography to afford the desired product S₄ 1.58 g as a colorless oil in 90% yield.

1H-NMR (600 MHz, CDCl₃): δ 8.99 (s, 1H), 2.18-2.13 (m, 1H), 1.97-1.94 (m, 1H), 1.84-1.73 (m, 4H), 1.37-1.28 (m, 2H), 1.1 (t, J = 6.0 Hz, 1H). 13C-NMR (150 MHz, CDCl₃): δ 200.7, 42.12, 28.57, 26.26, 24.54, 20.84, 15.39. IR (FT-IR): ν = 2941, 2868, 1684, 1450, 1288, 1227, 1192, 1153, 1040, 958, 930 cm⁻¹. MS (EI): m/z (%) = 110 (M⁺, 100), 95 (53), 81 (100), 67 (65), 41 (100). HRMS calcd for C₇H₁₀O: 110.0732. Found: 110.0728.

(2) Procedure for the Preparation of 1-(Bicyclo[3.1.0]hexan-1-yl)ethanone (S₆)

1-(Bicyclo[3.1.0]hexan-1-yl)ethanol (S₅)
Methylmagnesium bromide (15.0 mL, 3 M, 45.0 mmol) was dissolved in 270 mL anhydrous dimethyl ether under N₂, and then cooled to 0 °C. S₄ (45.0 mmol, in 10 mL Et₂O) was added slowly to the above solution. The solution was then stirred under 0 °C for 30 minutes before it was poured into the mixture of 100 g ice and 100 mL 1 M H₂SO₄(aq). After extracted with Et₂O, washed with water, and brine, dried over MgSO₄, and concentrated in vacuo, the crude mixture was purified by flash column chromatography to afford 3.4 g (60%) S₅ as a light yellow liquid.
1-(Bicyclo[3.1.0]hexan-1-yl)ethanone (S6)[5]

1-(Bicyclo[3.1.0]hexan-1-yl)ethanol S5 (3.4 g, 27.0 mmol) was dissolved in 100 mL anhydrous CH₂Cl₂ and cooled to 0 °C. Then PDC (11.1 g, 30 mmol) was added in batches and the resulting solution was stirred for 10 h at room temperature. The product mixture was filtered through a short silica gel column. Then the filtrate was concentrated to get the product with 70% yield (2.7 g) as a light yellow liquid.

(3) General Procedure for the Preparation of Vinyl Cyclopropyl Alcohols

Step 1: To a flask containing NaH (1.2 equiv.) and THF at 0 °C was added triethyl phosphonoacetate (1.2 equiv.). After stirring at room temperature for 30 min, the corresponding cyclopropyl carbonyl compound (1.0 equiv.) was added dropwise and the reaction was allowed to stir overnight. After quenching with brine, extracting with Et₂O, and drying over MgSO₄, concentration of the organic phase in vacuo gave a crude oil that was further purified by flash chromatography (petroleum ether/EtOAc = 9:1). 22 or 23 was obtained as a clear, colorless oil.

Step 2: To a Schlenk flask charged with ester 22 or 23 (1.0 equiv.) in THF at -78 °C was added DIBAL-H (1 M in toluene, 2.2 equiv.) dropwise. The reaction was warmed to room temperature overnight and was quenched with ethylacetate and aqueous potassium tartrate tetrahydrate. Stirring was continued until the solution was clear. Extracted with Et₂O, washed with brine, dried over MgSO₄, evaporation and purification by flash column chromatography (petroleum ether/EtOAc = 4:1) provided alcohol 24 or 25 as a clear, colorless oil.

Physical Data

(E)-Ethyl 3-(bicyclo[3.1.0]hexan-1-yl)acrylate (22)

$^1$H-NMR (600 MHz, CDCl₃): $\delta$ 6.80 (d, J = 15.6 Hz, 1H), 5.79 (d, J = 15.6 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 1.87-1.84 (m, 1H), 1.78-1.75 (m, 3H), 1.69-1.67 (m, 1H), 1.56-1.54 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 5.4 Hz, 1H), 0.87-0.84 (m, 2H). $^{13}$C-NMR (150 MHz, CDCl₃): $\delta$ 167.1, 155.2, 116.2, 59.9, 31.8, 29.1, 28.1, 27.0, 20.7, 16.9, 14.3. IR (FT-IR): $\nu$ = 2934, 2862, 1638, 1446, 1308, 1275, 1209, 1161, 1095, 1044, 983 cm⁻¹. MS (EI): m/z (%) = 180 (M⁺, 35), 151 (33), 79 (47), 43 (100). HRMS
(E)-Ethyl 3-(bicyclo[3.1.0]hexan-1-yl)but-2-enoate (23)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 6.74 (s, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 1.98-1.92 (m, 1H), 1.95 (s, 3H), 1.88 (d, $J = 1.8$ Hz, 1H), 1.84-1.78 (m, 1H), 1.73 (dd, $J = 12.0$ and 7.8 Hz, 1H), 1.68-1.63 (m, 1H), 1.40-1.38 (m, 1H), 1.28 (t, $J = 5.4$ Hz, 3H), 0.88-0.84 (m, 1H), 0.78 (t, $J = 4.8$ Hz, 1H), 0.67-0.64 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 168.8, 145.4, 127.9, 60.3, 31.2, 28.8, 27.5, 27.0, 21.3, 14.7, 14.3, 13.2. IR (FT-IR): $\nu$ = 2956, 2924, 1708, 1461, 1261, 1111, 1090, 745 cm$^{-1}$. MS (EI): m/z (%) = 194 (M$^+$, 95), 165 (77), 147 (63), 121(100), 79 (75). HRMS caled for C$_{12}$H$_{18}$O$_2$: 194.1307. Found: 194.1306.

(E)-3-(Bicyclo[3.1.0]hexan-1-yl)prop-2-en-1-ol (24)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.65-5.57 (m, 2H), 4.10 (d, $J = 5.4$ Hz, 2H), 1.86-1.81 (m, 1H), 1.77-1.69 (m, 3H), 1.66-1.61 (m, 1H), 1.53 (bs, 1H), 1.27-1.25 (m, 1H), 1.23-1.19 (m, 1H), 0.69 (t, $J = 4.8$ Hz, 1H), 0.59-0.57 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 138.8, 124.6, 63.8, 30.2, 29.2, 27.2, 26.6, 20.8, 14.5. IR (FT-IR): $\nu$ = 3327, 2932, 2860, 1664, 1451, 1040, 1006, 966 cm$^{-1}$. MS (EI): m/z (%) = 138 (M$^+$, 8.0), 120 (15), 91 (52), 79 (100), 41 (66). HRMS caled for C$_9$H$_{14}$O: 138.1045. Found: 138.1044.

(E)-3-(Bicyclo[3.1.0]hexan-1-yl)but-2-en-1-ol (25)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.52-5.49 (m, 1H), 4.18 (d, $J = 6.6$ Hz, 2H), 1.80-1.73 (m, 4H), 1.67 (bs, 1H), 1.60 (s, 3H), 1.39-1.37 (m, 1H), 1.27-1.22 (m, 2H), 0.62 (dd, $J = 8.4$ and 4.8 Hz, 1H), 0.54 (t, $J = 4.2$ Hz, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 142.2, 122.0, 59.6, 34.9, 30.8, 27.4, 23.8, 20.9, 14.3, 12.5. IR (FT-IR): $\nu$ = 3330, 2930, 2859, 1649, 1448, 1128, 997, 933 cm$^{-1}$. MS (EI): m/z (%) = 152 (M$^+$, 11), 123 (47), 93 (75), 79 (73), 43 (66). HRMS caled for C$_{10}$H$_{16}$O: 152.1201. Found: 152.1200.
(4) General Procedure for the Preparation of Geminal Diester-Tether Substrates 4, 6, and 14

Step 1: To a flask charged with NaH (1.8 equiv.) and THF at 0 °C was added dimethyl malonate (1.8 equiv.) dropwise. After stirred for 30 min, allyl iodide or allyl bromide (1.0 equiv.) was added and the reaction mixture was stirred at room temperature overnight. Quenching with brine, extracting with 
Et2O, drying over MgSO4, evaporation, and purification by flash column chromatography (petroleum ether/EtOAc = 9:1) provided I as a clear colorless oil.

Step 2: (a) To a 250 mL flask containing alcohol 24 or 25 (1.0 equiv.) in THF at -78 °C was added n-BuLi (1.6 M in hexane, 1.2 equiv.), followed 10 min later by methane sulfonyl chloride (1.2 equiv.), and then immediately by lithium bromide (4.5 equiv.) in one portion. The reaction mixture was stirred for 30 min. (b) To a second flask charged with NaH (1.6 equiv.) in THF was added I (1.6 equiv.) dropwise over 15 min. After stirred for 30 min at room temperature, the solution was cooled to -78 °C and the solution of the first flask was transferred in via cannula. The reaction mixture was stirred for 2 h at -78 °C, then allowed to warm to room temperature. Quenching with water, extracting with Et2O, drying over MgSO4, evaporation and purification by flash column chromatography (petroleum ether/EtOAc = 9:1) provided geminal diester derivatives 4, 6, and 14 as clear colorless oils.

Physical Data

(E)-Dimethyl 2-allyl-2-(3-(bicyclo[3.1.0]hexan-1-yl)allyl)malonate (4)

1H-NMR (600 MHz, CDCl3): δ 5.69-5.61 (m 1H), 5.42 (d, J = 15.6 Hz, 1H), 5.21-5.17 (m, 1H), 5.12-5.07 (m, 2H), 3.71(s, 6H), 2.65-2.58 (m, 4H), 1.76-1.75 ( m ,2H), 1.68-1.65 (m, 2H), 1.62-1.59 (m, 2H), 1.21-1.16 (m, 1H), 0.62 (t, J = 4.8 Hz, 1H), 0.51-0.49 (m, 1H). 13C-NMR (150 MHz, CDCl3): δ 171.5, 140.6, 132.7, 119.21, 119.17, 58.3, 52.5, 52.4, 37.2, 36.1, 30.7, 29.7, 27.4, 26.5, 21.1, 14.4. IR (FT-IR): ν = 2952, 2860, 1734, 1436, 1208, 994, 920, 858 cm⁻¹. MS (EI): m/z (%) = 292 (M⁺, 4.0), 219 (47), 120 (86), 91 (82), 79 (100). HRMS calcd for C17H24O4: 292.1675. Found: 292.1676.
(E)-Dimethyl 2-(3-(bicyclo[3.1.0]hexan-1-yl)allyl)-2-(2-methylallyl)malonate (6)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.40 (d, $J = 15.3$ Hz, 1H), 5.25-5.20 (m, 1H), 4.86-4.85 (m, 1H), 4.73 (t, $J = 6.0$ Hz, 1H), 3.69 (s, 6H), 2.69 (s, 2H), 2.61 (d, $J = 7.2$ Hz, 2H), 1.76-1.70 (m, 2H), 1.68-1.66 (m, 2H), 1.67 (s, 3H), 1.63-1.58 (m, 2H), 1.19-1.15 (m, 1H), 0.61 (t, $J = 4.8$ Hz, 1H), 0.51-0.48 (m, 1H).

$^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 171.5, 140.4, 139.9, 119.3, 115.4, 57.7, 51.9, 40.2, 35.8, 30.3, 29.4, 27.1, 26.1, 23.0, 20.7, 14.0. IR (FT-IR): $\nu$ = 2950, 2859, 1735, 1436, 1272, 1199, 1176, 968 cm$^{-1}$. MS (EI): m/z (%) = 306 (M$^+$, 5.0), 187 (36), 165 (34), 151(100), 120 (68), 79 (78). HRMS calcd for C$_{18}$H$_{26}$O$_4$: 306.1831. Found: 306.1845.

(5) General Procedure for the Preparation of Tosylamide-Tether Substrates 8, 10, 16, and 20

Step 1: To a flask was added TsNH$_2$ (1.1 equiv.), K$_2$CO$_3$ (1.5 equiv.) and acetone at 0 °C. After stirring for 30 min, allyl bromide or 4-bromobut-1-ene (1.0 equiv.) was added and the reaction mixture was refluxed for 7 h. Quenching with brine, extraction with Et$_2$O, drying over MgSO$_4$, evaporation, and purification by flash column chromatography (petroleum ether/EtOAc = 2:1) provided II as a white solid.

Step 2: To a solution of alcohol 24 or 25 (1.0 equiv.), II (1.2 equiv.), and PPh$_3$ (2.2 equiv.) in THF was
added DEAD (2.2 equiv.) at room temperature and the reaction mixture was stirred for 20 h at room
temperature. The resulting mixture was diluted with Et₂O, washed with water and brine, and dried over
Na₂SO₄. After removal of the solvent, the residue was purified by flash column chromatography with
Et₃N-impregnated silica gel (petroleum ether/EtOAc = 9:1) to give 8, 10, 16, and 20 as colorless oils.

Physical Data

\[ \text{(E)-N-Allyl-N-(3-(bicyclo[3.1.0]hexan-1-yl)allyl)-4-methylbenzenesulfonamide (8)} \]
\[ \text{H-NMR (600 MHz, CDCl}_3\text{):} \delta 7.69 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 5.66-5.59 (m, 1H), 5.39 (d, J = 10.2 Hz, 1H), 5.16-5.11 (m, 3H), 3.80-3.75 (m, 4H), 2.42 (s, 3H), 1.75-1.58 (m, 6H), 0.88-0.84 (m, 1H), 0.64 (t, J = 4.8 Hz, 1H), 0.48-0.47 (m, 1H). \]
\[ \text{13C-NMR (150 MHz, CDCl}_3\text{):} \delta 143.0, 141.0, 133.0, 129.5, 127.3, 119.4, 118.6, 49.0, 48.8, 30.2, 29.1, 27.2, 26.5, 21.5, 20.8, 14.4. IR (FT-IR): \nu = 2917, 2860, 1340, 1157, 1090, 912, 753 \text{ cm}^{-1}. \]
\[ \text{MS (EI): m/z (%) = 331 (M⁺, 2.0), 250 (18), 224 (38), 155 (48), 91 (100). HRMS calcd for C}_{19}\text{H}_{25}\text{NO}_{2}\text{S: 331.1606. Found: 331.1614.} \]

\[ \text{(E)-N-(3-(Bicyclo[3.1.0]hexan-1-yl)allyl)-N-(2-methylallyl)-4-methylbenzenesulfonamide (10)} \]
\[ \text{H-NMR (600 MHz, CDCl}_3\text{):} \delta 7.69 (d, J = 7.8 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 5.57-5.50 (m, 1H), 5.34 (d, J = 15.6 Hz, 1H), 5.06-4.84 (m, 2H), 3.74-3.67 (m, 4H), 1.70 (s, 3H), 1.69-1.53 (m, 6H), 0.60 (t, J = 4.8 Hz, 1H), 0.45-0.40 (m, 1H). \]
\[ \text{13C-NMR (150 MHz, CDCl}_3\text{):} \delta 142.9, 141.2, 140.4, 133.4, 129.2, 127.3, 118.9, 114.2, 52.5, 48.8, 30.2, 29.0, 27.2, 26.4, 21.5, 21.4, 20.8, 14.3. IR (FT-IR): \nu = 2927, 2859, 1337, 1156, 1089, 763 \text{ cm}^{-1}. \]
\[ \text{MS (EI): m/z (%) = 345 (M⁺, 4.0), 264 (16), 238 (38), 190 (46), 91 (100). HRMS calcd for C}_{20}\text{H}_{27}\text{NO}_{2}\text{S: 345.1763. Found: 345.1767.} \]

\[ \text{(E)-N-Allyl-N-(3-(bicyclo[3.1.0]hexan-1-yl)but-2-enyl)-4-methylbenzenesulfonamide (16)} \]
\[ \text{H-NMR (600 MHz, CDCl}_3\text{):} \delta 7.69 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 7.8 Hz, 2H), 5.69-5.63 (m, 1H), 5.15-5.11 (m, 2H), 5.01-4.98 (m, 1H), 3.83 (d, J = 6.6 Hz, 2H), 3.77 (d, J = 6.0 Hz, 2H), 2.42 (s, 3H), 1.70-1.68 (m, 2H), 1.64-1.60 (m, 2H), 1.59-1.58 (m, 2H), 1.57 (s, 3H), 0.89-0.83 (m, 2H), 0.47-0.45 (m, 1H). \]
\[ \text{13C-NMR (150 MHz, CDCl}_3\text{):} \delta 142.9, 142.5, 133.3, 129.53, 129.51, 127.2, 118.3, 117.1, 49.4, 44.6, 35.0, 30.8, 27.4, 23.6, 21.5, 20.9, 14.3, 12.3. IR (FT-IR): \nu = 2926, 2855, 1339, 1156, 1089, 1037, 922, 814, 756 \text{ cm}^{-1}. \]
\[ \text{MS (EI): m/z (%) = 345 (M⁺, 2.0), 238 (32), 224 (36), 155 (64), 91 (100), 41 (78).} \]
HRMS calcd for C$_{20}$H$_{27}$O$_2$S: 345.1763. Found: 345.1771.

(E)-N-(3-(Bicyclo[3.1.0]hexan-1-yl)allyl)-N-(but-3-enyl)-4-methylbenzenesulfonamide (20)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 7.69 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 7.8$ Hz, 2H), 5.74-5.68 (m, 1H), 5.44 (d, $J = 18$ Hz, 1H), 5.20-5.15 (m, 1H), 5.05-5.01 (m, 2H), 3.78-3.74 (m, 2H), 3.18-3.15 (m, 2H), 2.42 (s, 3H), 2.27 (q, $J = 6.6$ Hz, 2H), 1.73-1.58 (m, 6H), 1.19-1.18 (m, 1H), 0.64 (t, $J = 5.4$Hz, 1H), 0.49 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 143.2, 140.9, 137.7, 135.2, 129.7, 127.4, 120.2, 117.1, 50.3, 46.6, 33.3, 30.5, 29.4, 27.4, 26.7, 21.7, 21.0, 14.6. IR (FT-IR): $\nu$ = 2930, 2860, 1338, 1156, 1090, 1031, 926, 813, 746 cm$^{-1}$. MS (EI): m/z (%) = 345 (M$^+$, 6.0), 304 (12), 190 (14), 155 (20), 121 (100), 91 (68), 79 (58). HRMS calcd for C$_{20}$H$_{27}$O$_2$S: 345.1762. Found: 345.1757.

(6) General Procedure for the Preparation of Ether-Tethered Substrates 12 and 18

To a solution of NaH (1.2 equiv.) in THF was added a solution of alcohol 24 or 25 (1.0 equiv.) in THF at 0 °C and the mixture was refluxed for 2 h. The solution was cooled to room temperature, then allyl bromide (1.2 equiv.) was added and the mixture was refluxed overnight. After being cooled to room temperature, the reaction was quenched with water and extracted with Et$_2$O. Washed with brine, dried over MgSO$_4$, evaporation to remove the solvent, and purification by flash column chromatography (petroleum ether/EtOAc = 9:1) gave 12 and 18 as colorless oils.

Physical Data

(E)-1-(3-(2-Methylallyloxy)prop-1-enyl)bicyclo[3.1.0]hexane (12)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.61-5.53 (m, 2H), 4.96-4.95 (m, 1H), 4.89-4.88 (m, 1H), 3.91 (d, $J = 5.4$ Hz, 2H), 3.88(s, 2H), 1.87-1.82 (m, 1H), 1.74 (s, 3H), 1.72-1.68 (m, 2H), 1.64-1.60 (m, 2H), 1.27-1.20 (m, 2H), 0.68 (t, 1H), 0.59-0.57 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 142.6, 140.1, 122.2, 112.2, 74.1, 71.1, 30.5, 29.4, 27.5, 26.7, 21.1, 19.8, 14.8. IR (FT-IR): $\nu$ = 2929, 2859, 1450, 1113, 1077, 971, 891 cm$^{-1}$. MS (EI): m/z (%) = 192 (M$^+$, 12), 121 (32), 119 (42), 93 (74), 86 (100), 67
(E)-1-(4-(Allyloxy)but-2-en-2-yl)bicyclo[3.1.0]hexane (18)

$^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.94 (m, 1H), 5.45 (m, 1H), 5.27 (m, 1H), 5.17 (dd, $J = 10.2$ and 1.2 Hz, 1H), 4.01 (d, $J = 7.2$Hz, 2H), 3.96 (d, $J = 2.4$Hz, 2H), 1.81-1.78 (m, 2H), 1.77-1.69 (m, 2H), 1.62-1.59 (m, 2H), 1.59 (s, 3H), 1.25-1.20 (m, 1H), 0.62-0.60 (m, 1H), 0.26 (t, $J = 4.8$Hz, 1H).

$^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 142.5, 135.1, 119.5, 116.9, 71.1, 66.9, 35.0, 30.8, 27.5, 23.7, 21.0, 14.5, 12.5. IR (FT-IR): $\nu$ = 2926, 2860, 1450, 1066, 920, 800 cm$^{-1}$. MS (EI): m/z (%) = 192 (M$^+$, 6.0), 134 (22), 121 (30), 91 (38), 81 (48), 91 (68), 41 (100). HRMS calcd for C$_{13}$H$_{20}$O: 192.1514. Found: 192.1515.
3. General Procedure for the [(5 + 2) + 1] Cycloaddition Reactions

[Rh(CO)₂Cl]₂ (10 mol % to the substrate) was charged in a base-washed, oven-dried Schlenk flask under an atmosphere of nitrogen, and then a solution of the ene-VCP substrate in degassed dioxane (0.05 M) was added. The solution was bubbled with the mixed gas of CO and N₂ (0.2 atm CO + 0.8 atm N₂) for 5 min. The reaction mixture was stirred at 80 °C under balloon pressured mixed gas of CO and N₂ (0.2 atm CO + 0.8 atm N₂) until TLC indicated the completion of the reaction (72 h). After cooled to room temperature, the mixture was concentrated and the residue was purified by flash column chromatography with silica gel to afford the cycloaddition product.
4. Summary of all \((5 + 2 + 1)\) Cycloaddition Reactions

\[
\begin{align*}
&\text{MeOOC} & & & & \text{MeOOC} \\
&\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 54\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
&\text{MeOOC} & & & & \text{MeOOC} \\
&\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 61\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{TsN} & & & & \text{TsN} \\
\text{TsN} & & & & \text{TsN} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 72\% \text{ conversion, 58% yield} \\
73\% \text{ based on recovered starting material} & & & & \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{MeOOC} & & & & \text{MeOOC} \\
\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 37\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{MeOOC} & & & & \text{MeOOC} \\
\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 44\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{MeOOC} & & & & \text{MeOOC} \\
\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 62\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{MeOOC} & & & & \text{MeOOC} \\
\text{MeOOC} & & & & \text{MeOOC} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 67\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]

\[
\begin{align*}
\text{TsN} & & & & \text{TsN} \\
\text{TsN} & & & & \text{TsN} \\
\end{align*}
\]

\[
\begin{align*}
\text{dioxane, 0.05 M, 80 °C} & & \text{72h} & & 67\% \\
10 \text{ mol} \% \text{[Rh(CO)\(_2\)Cl\(_2\)]} & & 0.2 \text{ atm CO + 0.8 atm N\(_2\)} & & \\
\end{align*}
\]
10 mol% [Rh(CO)$_2$Cl]$_2$,
0.2 atm CO + 0.8 atm N$_2$

18

10 mol% [Rh(CO)$_2$Cl]$_2$,
0.2 atm CO + 0.8 atm N$_2$

20

dioxane, 0.05 M, 80 °C

72 h

66%

19a

19b

19a/19b = 1.5:1

21

72 h

30%
5. Physical Data for Cycloadducts

(3R*, 7R*, 11S*)-5,5-Bis(methoxycarbonyl)tricyclo[9.3.0.0^3,7]tetradec-1-ene-9-one (5)
Light yellow oil, 54% yield. $^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.28-5.24 (m, 1H), 3.74 (s, 3H), 3.73(s, 3H), 2.69-2.58 (m, 2H), 2.52-2.43 (m, 4H), 2.42-2.32 (m, 4H), 2.28-2.19 (m, 2H), 2.05-1.95 (m, 1H), 1.78-1.69 (m, 2H), 1.64-1.56 (m, 1H), 1.49-1.45 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 212.2, 173.1, 172.9, 147.5, 121.8, 59.0, 53.3, 52.82, 52.81, 43.2, 41.4, 41.0, 40.0, 39.5, 37.8, 34.5, 33.2, 24.1. IR (FT-IR): $\nu$ = 2916, 2848, 1731, 1434, 1245, 1166, 848 cm$^{-1}$. MS (EI): m/z (%) = 320 (M$^+$, 38), 302 (55), 203 (90), 91 (100), 79 (94), 41 (58). HRMS calcd for C$_{18}$H$_{24}$O$_5$: 320.1624. Found: 320.1621.

(3R*, 7R*, 11S*)-5,5-Bis(methoxycarbonyl)-7-methyltricyclo[9.3.0.0^3,7]tetradec-1-ene-9-one (7)
Yellow oil, 61% yield. $^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 5.39 (d, $J$ = 1.8 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.61-2.50 (m, 4H), 2.44-2.38 (m, 2H), 2.29-2.18(m, 2H), 2.03 (dd, $J$ = 13.8 and 9.0 Hz, 1H), 1.89-1.84 (m, 1H), 1.69-1.65 (m, 1H), 1.61-1.56 (m, 2H), 1.53-1.50 (m, 1H), 1.20 (s, 3H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 211.6, 173.9, 173.5, 147.4, 128.1, 57.9, 53.56, 53.53, 52.0, 51.2, 47.5, 47.1, 44.7, 41.2, 36.4, 35.3, 34.8, 26.4, 23.4. IR (FT-IR): $\nu$ = 2954, 2924, 1732, 1434, 1264, 1198, 1065, 847 cm$^{-1}$. MS (EI): m/z (%) = 334 (M$^+$, 84), 316 (100), 217 (40), 122 (46), 91 (52), 41(44). HRMS calcd for C$_{19}$H$_{26}$O$_5$: 334.1780. Found: 334.1772.

(3S*, 7S*, 11S*)-N-Tosyl-5-azatricyclo[9.3.0.0^3,7]tetradec-1-ene-9-one (9)
Light yellow oil, 72% conversion, 58% yield (79% based on recovered starting material). $^1$H-NMR (600 MHz, CDCl$_3$): $\delta$ 7.72 (d, $J$ = 7.8 Hz 2H), 7.34 (d, $J$ = 8.4 Hz, 2H), 4.96 (dd, $J$ = 8.4 and 1.8 Hz, 1H), 3.41 (d, $J$ = 10.2 Hz, 1H), 3.39 (d, $J$ = 9.6, 1H), 3.22 (dd, $J$ = 10.2 and 4.8 Hz, 1H), 2.82 (t, $J$ = 10.2 Hz, 1H), 2.61-2.47 (m, 3H), 2.45 (s, 3H), 2.42-2.33 (m, 3H), 2.32-2.16 (m, 3H), 1.99-1.96 (m, 1H), 1.73-1.70 (m, 1H), 1.62-1.58 (m, 1H), 1.48-1.47 (m, 1H). $^{13}$C-NMR (150 MHz, CDCl$_3$): $\delta$ 211.9, 149.5 144.3, 130.4, 128.1, 119.7, 54.5, 53.9, 51.8, 41.5, 39.6, 38.7, 35.2, 34.0, 30.4, 30.0, 24.8, 22.2. IR (FT-IR): $\nu$ = 2955, 2921, 1700, 1466, 1343, 1162, 1090, 1045, 803 cm$^{-1}$. MS (EI): m/z (%) = 359 (M$^+$, 24), 301 (90), 204 (78), 146 (72), 91 (100), 42 (86). HRMS calcd for C$_{20}$H$_{25}$NO$_3$S: 359.1555. Found:
(3S*, 7S*, 11S*)-N-Tosyl-7-methyl-5-azatricyclo[9.3.0.0^7]tetradec-1-ene-9-one (11)

Colorless crystals, 37% yield, m.p. 150 °C. 1H-NMR (600 MHz, CDCl_3): δ 7.73 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H), 4.83 (dd, J = 8.4 and 1.2 Hz, 1H), 3.34 (dd, J = 9.8 and 4.8 Hz, 1H), 3.31 (d, J = 10.2 Hz, 1H), 3.10 (d, J = 9.6 Hz, 1H), 2.91 (d, 9.0 Hz, 1H), 2.63 (d, J = 11.4 Hz, 1H), 2.57 (m, 1H), 2.45 (s, 3H), 2.40-2.30 (m, 3H), 2.28-2.19 (m, 3H), 1.97-1.90 (m, 1H), 1.72-1.67 (m, 1H), 1.60-1.57 (m, 1H), 1.44-1.42 (m, 1H), 0.87 (s, 3H). 13C-NMR (150 MHz, CDCl_3): δ 210.6, 149.0, 144.2, 134.9, 130.3, 127.9, 121.7, 59.3, 53.69, 53.66, 48.1, 47.5, 43.8, 38.0, 35.0, 33.4, 24.3, 23.9, 22.2. IR (FT-IR): ν = 2957, 2869, 1697, 1384, 1344, 1156, 1091, 1051, 738 cm^{-1}. MS (EI): m/z (%) = 373 (M^+, 30), 315 (60), 218 (78), 160 (94), 91 (76), 42 (100). HRMS calcd for C_{21}H_{27}NO_3S: 373.1711. Found: 373.1720. This structure was confirmed by X-ray crystallographic analysis.

(3S*, 7S*, 11S*)-7-Methyl-5-oxatricyclo[9.3.0.0^7]tetradec-1-ene-9-one (13)

Light yellow oil, 44% yield. 1H-NMR (600 MHz, CDCl_3): δ 5.38 (dd, J = 7.8 and 1.8 Hz, 1H), 4.13 (q, J = 13.8 Hz, 1H), 3.81 (d, J = 8.4 Hz, 1H), 3.52 (d, J = 7.2 Hz, 1H), 3.38 (d, J = 7.8 Hz, 1H), 2.71-2.68 (m, 2H), 2.53-2.37 (m, 5H), 2.03 (d, J = 11.4 Hz, 1H), 1.98-1.93 (m, 1H), 1.78-1.72 (m, 1H), 1.65-1.61 (m, 1H), 1.49-1.46 (m, 1H), 1.21 (s, 3H). 13C-NMR (150 MHz, CDCl_3): δ 210.9, 148.7, 123.5, 79.3, 75.0, 53.4, 48.7, 47.1, 44.7, 38.2, 35.0, 33.2, 24.4, 24.3. IR (FT-IR): ν = 2954, 2873, 1695, 1454, 1055, 882, 754 cm^{-1}. MS (EI): m/z (%) = 220 (M^+, 6.0), 162 (100), 135 (18), 91 (30), 79 (32), 41 (28). HRMS calcd for C_{14}H_{20}O_2: 220.1463. Found: 220.1473.

(3S*, 7S*, 11S*)-2-Methyl-5,5-bis(methoxylcarbonyl)tricyclo[9.3.0.0^7]tetradec-1-ene-9-one (15b)

Yellow oil, 62% yield. 1H-NMR (600 MHz, CDCl_3): δ 3.75 (s, 3H), 3.74 (s, 3H), 3.33-3.29 (m, 1H), 2.71-2.66 (m, 1H), 2.59-2.51 (m, 3H), 2.50-2.46 (m, 1H), 2.45-2.38 (m, 2H), 2.37-2.22 (m, 4H), 1.97-1.88 (m, 1H), 1.83-1.74 (m, 1H), 1.82-1.74 (m, 3H), 1.59 (s, 3H). 13C-NMR (150 MHz, CDCl_3): δ 211.2, 173.0, 172.9, 142.3, 125.7, 57.7, 52.9, 52.7, 52.6, 48.9, 45.2, 40.0, 39.2, 37.6, 37.4, 32.7, 29.6, 22.9, 15.4. IR (FT-IR): ν = 2954, 2923, 1731, 1435, 1257, 1199, 1066, 864 cm^{-1}. MS (EI): m/z (%) =
334 (M⁺, 94), 316 (82), 256 (54), 145 (82), 91 (80), 43 (100). HRMS calcd for C₁₉H₂₆O₅: 334.1780. Found: 334.1775.

Compound 15a is the minor product generated in the [(5+2)+1] cycloaddition, which is inseparable from the major product 15b. Therefore, no characterization data for 15a was provided.

(3S*, 7S*, 11S*)-2-Methyl-N-tosyl-5-azatricyclo[9.3.0.0³,7]tetradec-1-ene-9-one (17a)

Colorless crystals, 29% yield, m.p.154-155 °C. ¹H-NMR (600 MHz, CDCl₃): δ 7.71(d, J = 7.8 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 3.63 (d, J = 9.6 Hz, 1H), 3.48 (dd, J = 9.0 and 6.0 Hz, 1H), 3.18 (dd, J = 6.0 and 5.4 Hz, 1H), 2.86 (t, J = 7.2 Hz 1H), 2.82 (d, J = 10.8 Hz, 1H), 2.56 (d, J = 6.6 Hz, 1H), 2.52-2.46 (m, 1H), 2.30-2.34 (m, 1H), 2.27-2.22 (m, 2H), 2.09 (dd, J = 4.2 and 3.6Hz, 1H), 2.01-1.99 (m, 1H), 1.81-1.78 (m, 2H), 1.73-1.71 (m, 1H), 1.66 (s, 1H), 1.60-1.56 (m, 2H). ¹³C-NMR (150 MHz, CDCl₃): δ 211.8, 143.5, 142.7, 134.0, 129.8, 127.2, 123.5, 52.6, 51.4, 50.8, 43.9, 40.6, 40.0, 39.2, 34.8, 30.4, 23.0, 21.5, 16.2. IR (FT-IR): ν = 2955, 2922, 1697, 1378, 1342, 1160, 1094, 1055, 816 cm⁻¹. MS (EI): m/z (%) = 373 (M⁺, 42), 315 (10), 218 (100), 160 (48), 91 (78), 42 (50). HRMS calcd for C₂₁H₂₇NO₃S: 373.1711. Found: 373.1714. This structure was confirmed by X-ray crystallographic analysis.


White solid, 38% yield, m.p.142-144 °C. ¹H-NMR (600 MHz, CDCl₃): δ 7.71(d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 3.53 (d, J = 8.4 Hz, 1H), 3.45 (dd, J = 8.4 and 7.8 Hz, 1H), 3.27 (t, J = 10.5 Hz, 1H), 3.17 (t, J = 6.0 Hz, 1H), 2.99 (t, J = 9.9 Hz, 1H), 2.72 (dd, J = 8.4 Hz,1H), 2.54-2.51 (m, 1H), 2.48 (d, J = 10.8 Hz, 1H), 2.45 (s, 3H), 2.36-2.25 (m, 3H), 2.20-2.04 (m, 1H), 1.87 (m, 1H), 1.77-1.59 (m, 3H), 1.54-1.52 (m, 1H), 1.45 (s, 3H). ¹³C-NMR (150 MHz, CDCl₃): δ 209.8, 143.9, 143.5, 133.7, 129.7, 127.5, 123.1, 53.0, 52.2, 50.4, 48.1, 43.0, 39.0, 37.5, 32.6, 29.3, 22.3, 21.5, 15.7. IR (FT-IR): ν = 2955, 2922, 1697, 1378, 1342, 1160, 1094, 1055, 816 cm⁻¹. MS (EI): m/z (%) = 373 (M⁺, 42), 315 (10), 218 (100), 160 (48), 91 (78), 42 (50). HRMS calcd for C₂₁H₂₇NO₃S: 373.1711. Found: 373.1714.

(3S*, 7S*, 11S*)-2-Methyl-5-oxatricyclo[9.3.0.0³,7]tetradec-1-ene-9-one (19a)
Light yellow oil, 39% yield. \(^1\)H-NMR (600 MHz, CDCl\(_3\)): \(\delta\) 4.11 (d, \(J = 8.4\) Hz, 1H), 4.01 (t, \(J = 7.8\)Hz, 1H), 3.84 (dd, \(J = 5.4\) and 3.6 Hz, 1H), 3.21 (dd, \(J = 8.4\) Hz and 7.8, 1H), 2.94 (t, \(J = 12\)Hz, 1H), 2.70-2.68 (m, 1H), 2.57-2.46 (m, 2H), 2.38-2.36 (m, 2H), 2.38-2.36 (m, 2H), 2.26-2.20 (m, 2H), 2.19-1.74 (m, 3H), 1.71 (s, 3H), 1.67-1.57 (m, 2H). \(^{13}\)C-NMR (150 MHz, CDCl\(_3\)): \(\delta\) 212.1, 142.0, 124.0, 71.3, 71.0, 52.5, 45.2, 41.2, 40.0, 39.3, 34.9, 30.3, 23.0, 16.5. IR (FT-IR): \(\nu\) = 2946, 2860, 1689, 1438, 1047, 897, 754 cm\(^{-1}\). MS (EI): m/z (%) = 220 (M\(^+\), 50), 134 (48), 105 (60), 91 (87), 79 (68), 41 (100). HRMS calcd for C\(_{14}\)H\(_{20}\)O\(_2\): 220.1463. Found: 220.1468.

(3S\(^*\), 7R\(^*\), 11S\(^*\))-2-Methyl-5-oxatricyclo[9.3.0.0\(^3\),7\]tetradec-1-ene-9-one (19b)

Light yellow oil, 26% yield. \(^1\)H-NMR (600 MHz, CDCl\(_3\)): \(\delta\) 4.05 (t, \(J = 12\) Hz, 1H), 3.95 (t, \(J = 12\) Hz, 1H), 3.84 (dd, \(J = 12\) and 12.6 Hz, 1H), 3.43 (dd, \(J = 13.2\) Hz and 13.8 Hz, 1H), 2.98 (d, \(J = 13.2\) Hz, 1H), 2.69-2.60 (m, 2H), 2.42-2.30 (m, 2H), 2.28-2.16 (m, 1H), 2.15-2.00 (m, 1H), 1.62-1.56 (m, 2H), 1.53 (s, 3H). \(^{13}\)C-NMR (150 MHz, CDCl\(_3\)): \(\delta\) 210.4, 143.4, 124.1, 72.8, 70.7, 53.1, 49.9, 43.3, 41.0, 37.3, 32.5, 29.1, 22.3, 15.9. IR (FT-IR): \(\nu\) = 2946, 2860, 1689, 1438, 1047, 897, 754 cm\(^{-1}\). MS (EI): m/z (%) = 220 (M\(^+\), 50), 134 (48), 105 (60), 91 (87), 79 (68), 41 (100). HRMS calcd for C\(_{14}\)H\(_{20}\)O\(_2\): 220.1463. Found: 220.1468.

(3S\(^*\), 8R\(^*\), 12S\(^*\))-N-Tosyl-5-azatricyclo[10.3.0.0\(^3\),8\]pentadec-1-ene-10-one (21)

Colorless crystals, 30% yield, m.p.186 °C. \(^1\)H-NMR (600 MHz, CDCl\(_3\)): \(\delta\) 7.63 (d, \(J = 8.4\) Hz, 2H), 7.32 (d, \(J = 7.8\) Hz, 2H), 4.95 (dd, \(J = 8.4\) and 1.8 Hz, 1H), 3.80 (m, 1H), 3.73 (m, 1H), 3.01(m, 1H), 2.55 (dd, \(J = 12\) and 4.8 Hz, 1H), 2.49 (dd, \(J = 12\) and 5.4Hz, 1H), 2.44 (s, 3H), 2.40-2.36 (m, 1H), 2.32-2.23 (m, 3H), 2.20-2.15 (m, 2H), 2.01-1.60 (m, 5H), 1.63-1.49 (m, 1H), 1.31-1.26 (m, 1H), 0.89-0.83 (m, 1H). \(^{13}\)C-NMR (150 MHz, CDCl\(_3\)): \(\delta\) 212.1, 149.5, 144.1, 133.9, 130.4, 128.2, 120.9, 53.5, 51.8, 47.0, 46.8, 42.3, 38.1, 37.9, 33.8, 32.9, 31.6, 24.2, 22.2. IR (FT-IR): \(\nu\) = 2954, 2923, 1697, 1340, 1215, 1163, 1090 1022, 750 cm\(^{-1}\). MS (EI): m/z (%) = 373 (M\(^+\), 30), 316 (8.0), 218 (100), 198(28), 91 (56), 42 (34). HRMS calcd for C\(_{21}\)H\(_{24}\)NO\(_3\)S: 373.1712. Found: 373.1716. This structure was confirmed by X-ray crystallographic analysis.
6. X-Ray Structure for Cycloadducts 11, 17a, 21, and NOESY Correlations.

CCDC 673996, 756195, 673997 contain the supplementary crystallographic data for 11, 17a, and 21. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**Figure S1.** Chemical Structure and ORTEP Figure of Cycloadduct 11

![Chemical Structure and ORTEP Figure of Cycloadduct 11](image1)

**Figure S2.** Chemical Structure and ORTEP Figure of Cycloadduct 17a

![Chemical Structure and ORTEP Figure of Cycloadduct 17a](image2)

**Figure S3.** Chemical Structure and ORTEP Figure of Cycloadduct 21

![Chemical Structure and ORTEP Figure of Cycloadduct 21](image3)
**Figure S4.** Selected NOESY Correlations for 5.

![Figure S4](image)

**Figure S5.** Selected NOESY Correlations for 7.

![Figure S5](image)

**Figure S6.** Selected NOESY Correlations for 9.

![Figure S6](image)

**Figure S7.** Selected NOESY Correlations for 13.

![Figure S7](image)
**Figure S8.** Stereochemistry Assignment for 15a/b.

Since the carbonyl carbons in trans compounds have lower $^{13}$C NMR shift compared to those in the cis compounds (19b vs. 19a, 17b vs. 17a), we assigned the major product in 15a/b is 15b, which has a trans configuration. The ratio of 15a/15b is determined by $^1$H NMR.

**Figure S9.** Selected NOESY Correlations for 19a.
7. Stereochemistry Determination

Compounds 5, 7, 9, 13, and 19a have a cis-fused A/B rings system and this assignment is supported by NOESY experiments. The stereochemistry of compound 7 was deduced by analogy to 11. Compounds 15b and 19b have a trans-fused A/B rings system. This is deduced by analogy to the previous experimental findings (Y. Wang, J. Wang, J. C. Su, F. Huang, L. Jiao, Y. Liang, D. Z. Yang, S. W. Zhang, P. A. Wender, Z.-X. Yu, J. Am. Chem. Soc. 2007, 129, 10060). The assignment of the structure of 15b was mainly based on $^{13}$C NMR (see section 6 above). The configuration between the substituents at positions II and III is cis, as shown by XRD analysis of cycloadducts 11, 17a, and 21. This can be well understood based on the computational model, thus, all the [(5+2)+1] cycloadducts were assigned to the same cis configuration for the substituents at positions II and III.
8. DFT Calculations and Cartesian Coordinates of Computed Species

**Computational Details.** All of the calculations were performed with the Gaussian 03 program. B3LYP functional was used to locate all the transition structures and intermediates. 6-31G* basis set is applied for all elements except for Rh, which uses the basis set of LANL2DZ+ECP. This method has been successfully applied to predict structures and reaction mechanisms for reactions of dirhodium tetracarboxylate complexes and other Rh-catalyzed cycloadditions. Frequency calculations at the same level have been performed to confirm each stationary point to be either a minimum or a transition structure. The reported energies are Zero-point energy-corrected electronic energies ($\Delta E_{0 K}$), enthalpies ($\Delta H_{298 K}$), and Gibbs free energies ($\Delta G_{298 K}$).

**Table S1.** The Computed Energies and Other Thermal Parameters for the Three-Component [(5+2)+1] Reaction (in Hartree)

<table>
<thead>
<tr>
<th>Structure</th>
<th>$E_{ele}$</th>
<th>$E_{0 K}$</th>
<th>$H_{298 K}$</th>
<th>$G_{298 K}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>-1034.237214</td>
<td>-1034.4569113</td>
<td>-1034.222700</td>
<td>-1034.279901</td>
</tr>
<tr>
<td>TS</td>
<td>-1034.223202</td>
<td>-1034.4409475</td>
<td>-1034.208968</td>
<td>-1034.265139</td>
</tr>
<tr>
<td>S1a</td>
<td>-1034.232408</td>
<td>-1034.450763</td>
<td>-1034.217636</td>
<td>-1034.275472</td>
</tr>
</tbody>
</table>

**S1:**

<table>
<thead>
<tr>
<th>Element</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>-3.949464</td>
<td>0.107980</td>
<td>-0.338061</td>
</tr>
<tr>
<td>C</td>
<td>-3.623324</td>
<td>-0.716143</td>
<td>0.929695</td>
</tr>
<tr>
<td>C</td>
<td>-2.298877</td>
<td>-0.126013</td>
<td>1.463275</td>
</tr>
<tr>
<td>C</td>
<td>-1.581837</td>
<td>0.450140</td>
<td>0.237762</td>
</tr>
<tr>
<td>C</td>
<td>-2.590310</td>
<td>0.529405</td>
<td>-0.885573</td>
</tr>
<tr>
<td>C</td>
<td>-1.533615</td>
<td>-0.536514</td>
<td>-1.010051</td>
</tr>
<tr>
<td>C</td>
<td>-0.432100</td>
<td>1.364175</td>
<td>0.457246</td>
</tr>
<tr>
<td>C</td>
<td>0.345945</td>
<td>1.894117</td>
<td>-0.584199</td>
</tr>
<tr>
<td>Rh</td>
<td>0.896213</td>
<td>-0.197757</td>
<td>-0.114266</td>
</tr>
<tr>
<td>O</td>
<td>3.568510</td>
<td>0.428140</td>
<td>1.033618</td>
</tr>
<tr>
<td>C</td>
<td>2.537656</td>
<td>0.182668</td>
<td>0.578320</td>
</tr>
<tr>
<td>Cl</td>
<td>1.397667</td>
<td>-2.491898</td>
<td>-0.349142</td>
</tr>
<tr>
<td>H</td>
<td>-0.009496</td>
<td>1.794917</td>
<td>-1.610730</td>
</tr>
<tr>
<td>C</td>
<td>1.330364</td>
<td>3.018330</td>
<td>-0.376903</td>
</tr>
<tr>
<td>H</td>
<td>-0.298529</td>
<td>1.738617</td>
<td>1.470398</td>
</tr>
<tr>
<td>H</td>
<td>-1.692857</td>
<td>-0.860984</td>
<td>2.002663</td>
</tr>
<tr>
<td>H</td>
<td>-2.499208</td>
<td>0.705518</td>
<td>2.152354</td>
</tr>
<tr>
<td>H</td>
<td>-4.425390</td>
<td>-0.671937</td>
<td>1.672204</td>
</tr>
</tbody>
</table>
H  -3.490297  -1.772268   0.672367
H  -4.520305   1.008981  -0.080060
H  -4.541535  -0.458522  -1.065921
H  -2.541984  1.353903  -1.592664
H  -1.775503  -1.579205  -0.833947
H  -0.814242  -0.388467  -1.817963
H   2.204223   2.907585  -1.027105
H   0.861533   3.981499  -0.621974
H   1.678963   3.067739   0.659771

-----------------------------------------

TS:

C  -1.152627  -0.702760  -1.207171
C  -1.463327   0.584989   0.324166
Rh  0.735349  -0.171359  -0.139513
Cl  1.271546  -2.506598  -0.254187
C  -2.267339   0.271750  -0.903203
C  -3.620746  -0.302724  -0.420411
C  -3.643308  -0.050131   1.106972
C  -2.155436  -0.046453   1.521803
C  -0.395917   1.537415   0.434792
C   0.367025   1.924348  -0.692407
C   1.459072   2.958146  -0.606116
O   3.428990   0.249494   1.274248
C   2.436561   0.114712   0.712135
H   2.274149   2.727570  -1.300231
H   1.069912   3.949383  -0.878970
H   1.878449   3.024813   0.403076
H  -0.077853   1.822468  -1.681599
H  -0.149342   1.915100   1.424296
H  -1.792321  -1.067433   1.681507
H  -1.948123   0.512609   2.440749
H  -4.084023   0.932301   1.316547
H  -4.229853  -0.794658   1.653602
H  -4.466923   0.171800  -0.926409
H  -3.672980  -1.374987  -0.640044
<table>
<thead>
<tr>
<th>Atoms</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>-2.353034</td>
<td>1.086943</td>
<td>-1.624149</td>
</tr>
<tr>
<td>H</td>
<td>-1.325631</td>
<td>-1.735420</td>
<td>-0.919194</td>
</tr>
<tr>
<td>H</td>
<td>-0.645069</td>
<td>-0.578858</td>
<td>-2.167279</td>
</tr>
</tbody>
</table>

S1a:

<table>
<thead>
<tr>
<th>Atoms</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>-2.049183</td>
<td>-0.311600</td>
<td>-0.879838</td>
</tr>
<tr>
<td>C</td>
<td>-0.820993</td>
<td>-1.160525</td>
<td>-1.217556</td>
</tr>
<tr>
<td>C</td>
<td>-0.538734</td>
<td>1.681786</td>
<td>-0.179643</td>
</tr>
<tr>
<td>C</td>
<td>0.331143</td>
<td>1.496991</td>
<td>-1.301968</td>
</tr>
<tr>
<td>Rh</td>
<td>0.586421</td>
<td>-0.201884</td>
<td>-0.006904</td>
</tr>
<tr>
<td>C</td>
<td>1.512204</td>
<td>2.397445</td>
<td>-1.540314</td>
</tr>
<tr>
<td>Cl</td>
<td>1.932887</td>
<td>-2.141509</td>
<td>-0.125635</td>
</tr>
<tr>
<td>O</td>
<td>2.701675</td>
<td>0.893194</td>
<td>2.105782</td>
</tr>
<tr>
<td>C</td>
<td>1.919391</td>
<td>0.591602</td>
<td>1.327164</td>
</tr>
<tr>
<td>H</td>
<td>1.904859</td>
<td>2.816391</td>
<td>-0.607946</td>
</tr>
<tr>
<td>H</td>
<td>1.225356</td>
<td>3.232016</td>
<td>-2.196975</td>
</tr>
<tr>
<td>H</td>
<td>2.318933</td>
<td>1.851951</td>
<td>-2.040629</td>
</tr>
<tr>
<td>H</td>
<td>-0.089979</td>
<td>1.066885</td>
<td>-2.208207</td>
</tr>
<tr>
<td>H</td>
<td>-0.887421</td>
<td>-2.191281</td>
<td>-0.864999</td>
</tr>
<tr>
<td>H</td>
<td>-0.519231</td>
<td>-1.150294</td>
<td>-2.268039</td>
</tr>
<tr>
<td>H</td>
<td>-0.300900</td>
<td>2.446424</td>
<td>0.558895</td>
</tr>
<tr>
<td>C</td>
<td>-1.513922</td>
<td>0.726153</td>
<td>0.124982</td>
</tr>
<tr>
<td>C</td>
<td>-2.366305</td>
<td>0.724702</td>
<td>1.377582</td>
</tr>
<tr>
<td>C</td>
<td>-3.673094</td>
<td>0.042224</td>
<td>0.917593</td>
</tr>
<tr>
<td>C</td>
<td>-3.188647</td>
<td>-1.009688</td>
<td>-0.097534</td>
</tr>
<tr>
<td>H</td>
<td>-2.467938</td>
<td>0.206451</td>
<td>-1.755184</td>
</tr>
<tr>
<td>H</td>
<td>-1.883538</td>
<td>0.123601</td>
<td>2.159678</td>
</tr>
<tr>
<td>H</td>
<td>-2.505353</td>
<td>1.731947</td>
<td>1.786940</td>
</tr>
<tr>
<td>H</td>
<td>-4.321896</td>
<td>0.777367</td>
<td>0.423955</td>
</tr>
<tr>
<td>H</td>
<td>-4.238673</td>
<td>-0.389671</td>
<td>1.749078</td>
</tr>
<tr>
<td>H</td>
<td>-3.983576</td>
<td>-1.372965</td>
<td>-0.755944</td>
</tr>
<tr>
<td>H</td>
<td>-2.783202</td>
<td>-1.878484</td>
<td>0.436809</td>
</tr>
</tbody>
</table>
9. References

[9] Each d orbital (for all elements) includes 5d functions (the keyword used in the Gaussian 98 calculations is 5D, 7F).
10. $^1$H and $^{13}$C Spectra for all New Compounds