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Rh(I)-Catalyzed Chemo- and Stereoselective Domino Cycloaddition of Optically Active Propargyl 2,4-Hexadienyl Ethers

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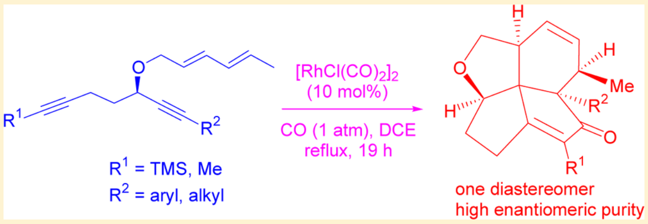
Supporting Information



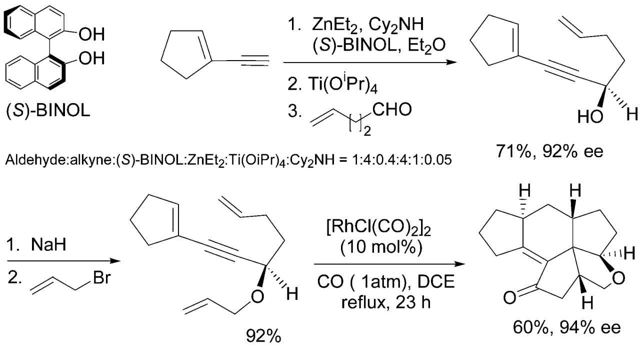
ABSTRACT: 1,1′-Bi-2-naphthol in combination with $ZnEt_2$, $Ti(O^iPr)_4$, and dicyclohexylamine have been employed to catalyze asymmetric alkyne addition to an ynal to synthesize optically active propargylic alcohols containing two alkyne functions with excellent yields and enantioselectivities. These chiral alcohols are readily converted to the corresponding optically active propargyl 2,4-hexadienyl ethers. These dienediyne substrates are found to undergo a highly chemoselective and stereoselective domino Pauson–Khand and Diels–Alder cycloaddition catalyzed by $[RhCl(CO)_2]_2$ under CO to generate a class of tetracyclic compounds with high enantiomeric purity. This is a very efficient method for the asymmetric synthesis of polycyclic compounds.

INTRODUCTION

Over the past decade, significant progress has been made on the catalytic asymmetric alkyne addition to aldehydes to generate chiral propargylic alcohols.[1−3] For example, in our laboratory, we have discovered that the readily available 1,1′-bi-2-naphthol (BINOL) in combination with $ZnEt_2$ and $Ti(O^iPr)_4$ can catalyze the highly enantioselective reaction of a broad range of alkynes with aldehydes.[3] Addition of a catalytic amount of dicyclohexylamine (Cy_2NH) allows the entire catalytic process to be conducted at room temperature.[3c,d] Using the BINOL-based catalytic system can quickly produce structurally diverse chiral propargylic alcohols with high enantiomeric purity. This has prompted us to explore the application of these chiral propagylic alcohols in the asymmetric synthesis of multicyclic organic compounds.[4]

Scheme 1 shows an example of a Rh(I)-catalyzed domino cyclization of a chiral propargylic alcohol derivative we recently reported.[4a] A chiral propargylic alcohol was obtained from the BINOL-based catalytic enyne addition to an aldehyde with high enantiomeric purity. After preparation of its allylic ether, it was treated with a Rh(I) catalyst under CO, which catalyzed a domino cycloaddition to give a multicyclic product. In this paper, we report our further development of this strategy by conducting the Rh(I)-catalyzed domino cyclization of chiral propargyl 2,4-hexadienyl ethers. This process efficiently generates multicyclic products with high diastereoselectivity and high enantiomeric purity.

Scheme 1. BINOL-Catalyzed Enyne Addition to an Aldehyde and Catalytic Conversion of a Chiral Propargyl Allyl Ether to a Pentacyclic Product



RESULTS AND DISCUSSION

Preparation of Chiral Propargylic Alcohols by the Catalytic Asymmetric Alkyne Addition to Aldehydes and Their Conversion to 2,4-Hexadienyl Ethers. We have conducted the asymmetric alkyne addition to 5-(trimethylsilanyl)pent-5-ynal to synthesize a series of chiral propargylic alcohols containing two alkyne functions. As shown in Table 1, in the presence of (*S*)-BINOL, $ZnEt_2$, Cy_2NH, and $Ti(O^iPr)_4$, the reaction of various terminal alkynes with the ynal gave the corresponding diynols (*R*)-**1a**−**g** with good yields (69−95%) and high enantioselectivity (86−92% ee). Both the aromatic alkynes and aliphatic alkynes show similarly high stereoselectivity. These reactions were conducted in diethyl ether solution at room temperature under nitrogen in a three-step−one-pot process. In the first step, an alkyne was treated with $ZnEt_2$, Cy_2NH, and (*S*)-BINOL, which presumably generated a nucleophilic alkynylzinc reagent. The Lewis base Cy_2NH could increase the basicity of Et_2Zn for the deprotonation of the alkyne. In the second step, the deprotonated (*S*)-BINOL in the first step was combined with $Ti(O^iPr)_4$ to generate a chiral

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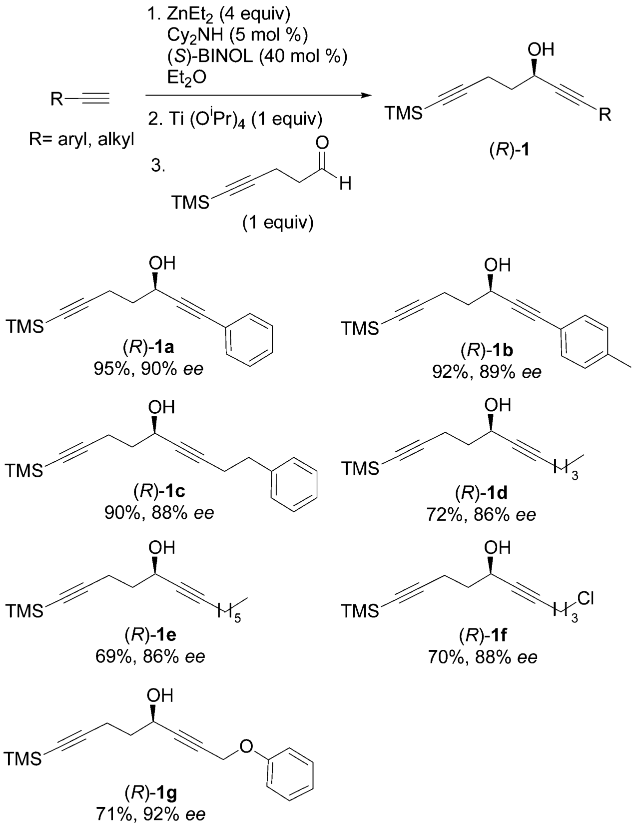
Table 1. Catalytic Asymmetric Alkyne Addition to Aldehydes To Form Chiral Propargylic Alcohols

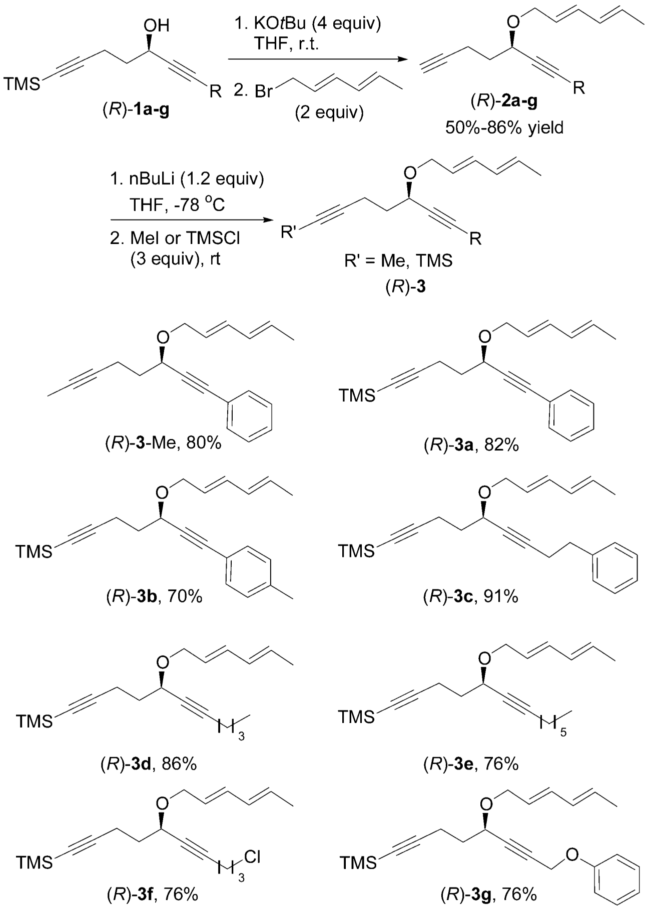


Lewis acid catalyst. In the third step, an aldehyde was added and the asymmetric alkyne addition proceeded. After aqueous workup, the desired chiral propargylic alcohol product was obtained.

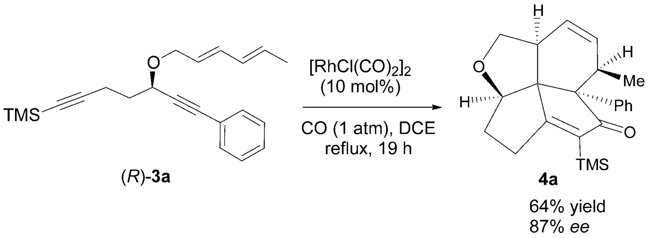
We have introduced conjugated diene unit into the above optically active diynols by reacting with 1-bromo-2,4-hexadiene under basic conditions. As shown in Table 2, treatment of (*R*)-**1a**−**g** with ^{t}BuOK followed by addition of 1-bromo-2,4-hexadiene at room temperature gave the corresponding ether products (*R*)-**2a**−**g** in 50−86% yield. In this step, the TMS group was also removed. This allows the introduction of other groups on the alkyne unit. For example, treatment of (*R*)-**2a** with ^{n}BuLi followed by addition of MeI gave the methylated product (*R*)-**3**-Me. The TMS group was also placed back on the alkyne unit to give compounds (*R*)-**3a**−**g** in good yields. Compounds (*R*)-**3** are optically active propargyl 2,4-hexadienyl ethers containing two alkyne functions and a conjugated diene. These compounds are designed to undergo a metal-promoted domino Pauson−Khand and Diels−Alder cycloaddition.

Catalytic Domino Pauson−Khand (PK) and Diels−Alder (DA) Cycloaddition of the Optically Active Diene-Diyne Ethers. With the synthesis of the optically active diene-diyne ethers, we studied their catalytic conversions in the presence of a Rh(I) catalyst and CO. When the optically active dienediyne (*R*)-**3a** was treated with 10 mol % of $[RhCl(CO)_2]_2$ under 1 atm of CO in refluxing 1,2-dichloroethane (DCE), a highly chemoselective and stereoselective domino PK/DA cycloaddition occurred to generate the tetracyclic product **4a** as a single diastereomer with 64% yield and 87% ee (Scheme 2). This demonstrates that the enantiomeric purity of the original chiral propargylic alcohol (*R*)-**1a** generated by the catalytic asymmetric alkyne addition to aldehydes is almost completely maintained. There is little change in the enantiomeric purity in the ether formation step as well as in the domino cyclization step. In this domino cycloaddition process, four new chiral centers including a quaternary chiral carbon core are formed.

Table 2. Preparation of the Chiral Propargylic Ether Based Dienediynes



Scheme 2. Catalytic Conversion of (*R*)-3a To Generate 4a



The structure of **4a** was established by high-resolution mass spectroscopic analysis and various ^{1}H and ^{13}C NMR spectroscopic analyses, including COSY, NOESY, HSQC, and DEPT-135 (Figure 1). In the ^{1}H NMR spectrum of **4a**, the signals at δ 3.61 (d, 1H, J = 3.2 Hz), 3.75 (dd, 1H, J = 12.8, 8 Hz), and 4.16 (t, 1H, J = 7.2 Hz) are attributed to H$_1$, H$_2$, and H$_3$, respectively. The ^{1}H NMR signal of H$_{11}$ at δ 1.07 is shifted unusually upfield in comparison with that of H$_{10}$ at δ 2.08 on the same carbon. We attribute this to the shielding effect of the Ph group of **4a** on H$_{11}$. In the ^{13}C NMR spectrum, the carbonyl signal of **4a** is observed at δ 211.5 and the TMS-substituted vinyl carbon signal is observed at δ 192.6. The carbon bearing H$_1$ gives a signal at δ 80.9 and that bearing H$_2$ and H$_3$ at δ 69.7.

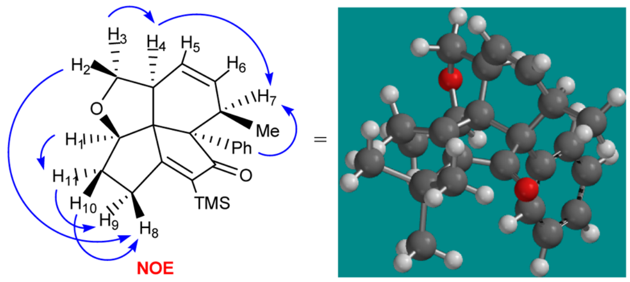


Figure 1. Observed NOE effects of compound **4a** and a molecular modeling structure.

The two quaternary carbons in the core give signals at δ 74.2 and 65.6, respectively. Figure 1 shows the observed NOE effects between the proton signals which have allowed the determination of its stereo structure. More detailed signal assignments are included in the Supporting Information. A molecular modeling structure of **4a** obtained by using the Spartan semiempirical PM3 program is shown in Figure 1.

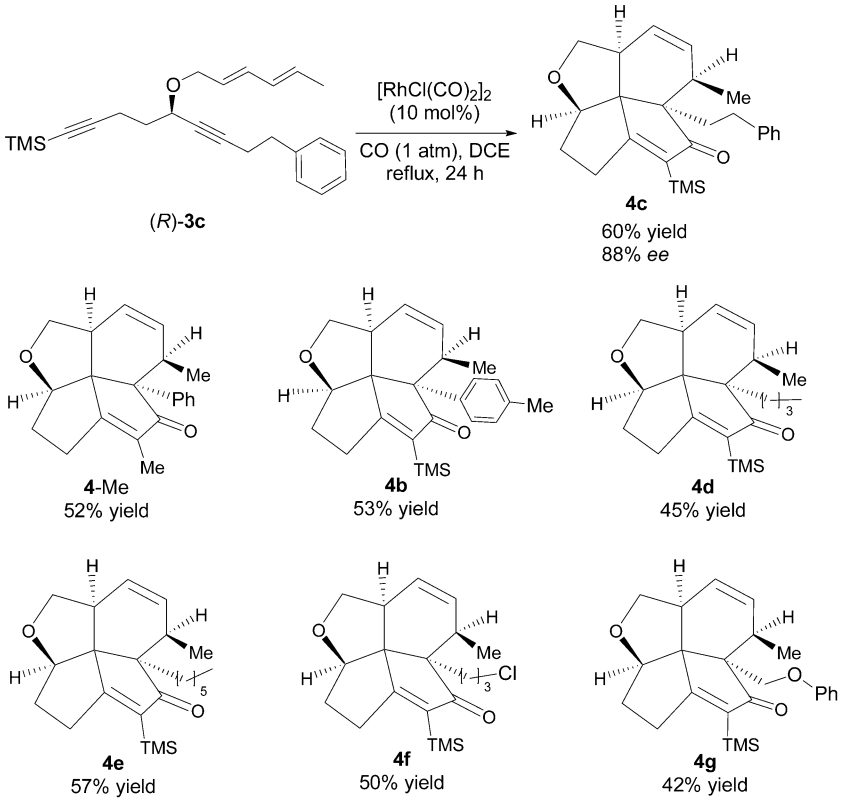
Previously, Chung reported a Co-catalyzed cyclization of racemic dienediynes to give racemic tetracyclic products similar to **4a**.[5] The use of the Co catalyst required higher temperature (130 °C) and higher pressure (30 atm) of CO in comparison to those for the use of the Rh catalyst reported here. In Chung's work, the stereostructure of the product is also different from that of **4a**, which could be due to either a different reaction mechanism or a possible error in assignment.

When the aliphatic alkyne derived propargylic ether (*R*)-**3c** was treated with the Rh(I) catalyst under the same conditions as the reaction of (*R*)-**3a**, a similar tetracyclic product **4c** was also obtained as a single diastereomer with 60% yield and 88% ee (Table 3). Thus, the enantiomeric purity of the starting chiral propargylic alcohol (*R*)-**1c** is completely maintained in this product. In a similar fashion, the other propargylic ethers (*R*)-**3** are also converted to the corresponding cyclic products **4** in the presence of $[RhCl(CO)_2]_2$ and CO with high chemoselectivity and stereoselectivity. It is expected that these products should also maintain the enantiomeric purity of their corresponding propargylic alcohol starting materials, similar to the case for **4a,c**.

Single crystals of compound **4d** were obtained by slow evaporation of its hexane/isopropyl alcohol solution. An X-ray analysis of these single crystals has allowed us to determine the structure of **4d**, as shown in Figure 2. This confirms the structural assignment derived by analogy with that of **4a** determined by NMR analysis. The bond angles around the central quaternary carbon of **4d** are found to be 100.0−116.6° with the angle C(2)−C(1)−C(9) being the largest and the angle C(2)−C(1)−C(12) being the smallest. These data are very close to those calculated for **4a**.

The reactions of additional racemic propargylic ether substrates in the presence of $[RhCl(CO)_2]_2$ and CO were also studied (Figure 3). Under the same conditions, compound **2a** with a terminal alkyne group gave a complicated product mixture. Apparently other reactions also occurred on the terminal alkyne. Compound **3i** was observed to undergo the domino PK/DA cycloaddition in the presence of $[RhCl(CO)_2]_2$ and CO. However, unlike (*R*)-**3**-Me, which gave **4**-Me as a single diastereomer, **3i** gave a mixture of two inseparable diastereomers in about a 1.6:1 ratio. When the bis-TMS compound **3j** was subjected to the reaction conditions, an enyne PK cycloaddition took place to give **4j** in 51% yield. That is, the PK cycloaddition of the two TMS group substituted

Table 3. Synthesis of More Tetracyclic Products 4 from the Rh(I)-Catalyzed Domino PK/DA Cycloaddition



(*R*)-**3c**

4c
60% yield
88% *ee*

4-Me
52% yield

4b
53% yield

4d
45% yield

4e
57% yield

4f
50% yield

4g
42% yield

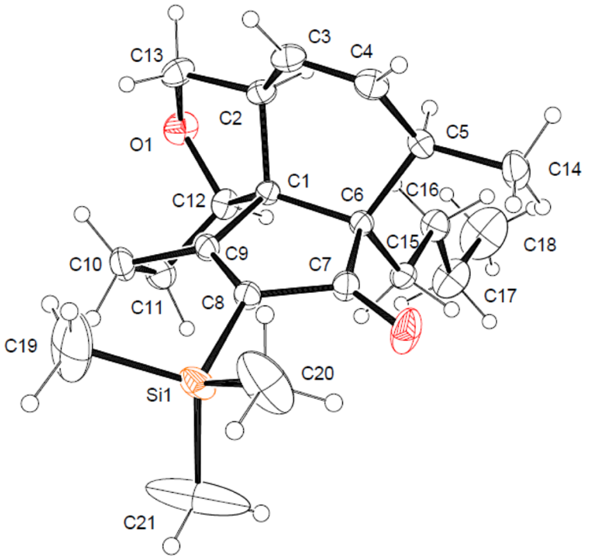


Figure 2. Structure of compound **4d** determined by X-ray analysis.

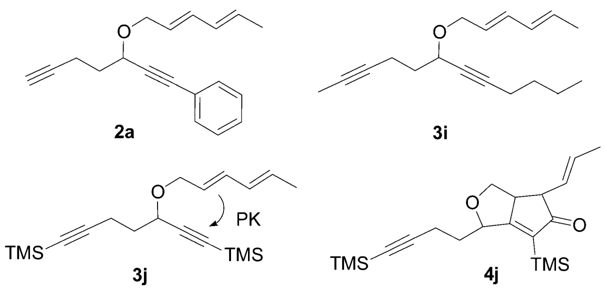


Figure 3. Additional diene-diyne substrates studied.

alkyne units might be too sterically hindered to occur. This shows that it is possible to control the direction of the cycloaddition by varying the substituents of the alkyne units to generate diverse products. The formation of **4j** from **3j** also suggests that the intramolecular DA reaction of the alkyne unit with the conjugated diene should not occur prior to the PK cycloaddition of the diyne unit. That is, the PK cycloaddition of compounds **3** should be more facile than the DA cycloaddition under the reaction conditions.

On the basis of previous studies on the Rh-catalyzed PK reactions,[4a,b,6] a mechanism is proposed to illustrate the formation of compound **4a** from (*R*)-**3a** (Scheme 3). Coordination of (*R*)-**3a** with $[RhCl(CO)_2]_2$ can generate the intermediate **5**. Oxidative coupling of the coordinated triple bonds of **5** gives **6**. Migratory insertion of **6** with CO followed by reductive elimination should give the PK cycloaddition product **7**. When both of the alkyne units contain a TMS group, as in **3j**, it should be more difficult to generate a corresponding intermediate similar to **5** due to the steric interaction of the two bulky TMS groups in the intermediate, and thus no PK cycloaddition of the two alkyne units of **3j** was observed. The cyclopentadienone unit of the intermediate **7** is expected to be highly reactive, which readily undergoes an intramolecular endo-DA cycloaddition to give the tetracyclic product **4a**. In this step, the cis H_β and H_γ atoms on the newly formed chiral centers are cis with respect to H_α on the propargylic chiral center, whereas Ph and Me are trans with respect to each other. The stereochemistry of the isolated product supports this mechanism.

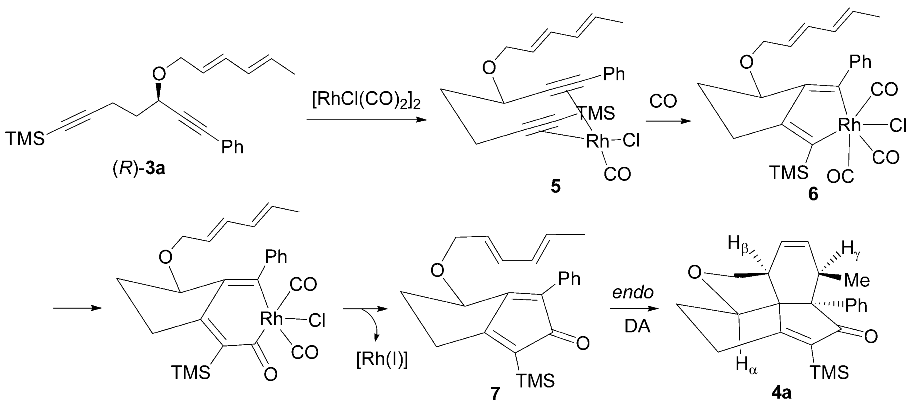
Conclusion. Using the chiral propargylic alcohols prepared from the catalytic asymmetric alkyne addition to aldehydes, we have synthesized a series of optically active propargyl 2,4-hexadienyl ethers. These compounds are found to undergo a one-pot Rh(I)-catalyzed intramolecular domino PK/DA cycloaddition under mild reaction conditions to generate optically active tetracyclic products with high chemoselectivity and stereoselectivity. We have demonstrated that the high enantiomeric purity of the propargylic alcohols generated from the catalytic asymmetric alkyne addition is maintained in the domino cycloaddition products. This strategy is very efficient for the asymmetric synthesis of polycyclic compounds.

■ EXPERIMENTAL SECTION

General Data. All commercial chemicals were used without further purification unless otherwise noted. All catalysts were purchased and stored under a dry nitrogen atmosphere. Tetrahydrofuran was distilled over sodium and benzophenone under nitrogen. Diethyl ether and methylene chloride were dried by passing through activated alumina columns under nitrogen. All the NMR spectra were obtained in $CDCl_3$ unless indicated otherwise.

General Procedure for the Catalytic Asymmetric Alkyne Addition to Aldehydes. Under nitrogen, (*S*)-BINOL (40 mol %) was weighed into a tared flask and dissolved in Et_2O (9 mL). An alkyne (4 equiv), Cy_2NH (5 mol %), and Et_2Zn (4 equiv) were added, and the mixture was stirred at room temperature for 16 h. Then, $Ti(O^iPr)_4$ (1 equiv) was added and stirring was continued for 3 h. An aldehyde (0.75 mmol, 1 equiv) was added and the mixture was stirred for another 4 h. The reaction mixture was quenched with saturated aqueous ammonium chloride and extracted three times with CH_2Cl_2.

Scheme 3. Proposed Mechanism for the Chemoselective and Stereoselective Domino PK/DA Cycloadditions



The organic layer was dried with anhydrous Na_2SO_4 and concentrated by rotary evaporation. The resultant oil was purified by flash column chromatography on silica gel with hexanes/ethyl acetate to give the propargylic alcohol products with 69−95% yield and 86−92% ee.

Characterization of the Chiral Propargylic Alcohol Products (*R*)-1a−g Generated from Alkyne Additions to Aldehydes. *(R)-1-Phenyl-7-(trimethylsilyl)hepta-1,6-diyn-3-ol ((R)-**1a**).* Light yellow oil, 182.4 mg, 95% yield. 90% ee determined by HPLC analysis: CHIRALCEL OD column, 98/2 hexanes/^{i}PrOH, flow rate 1.0 mL/min, λ 254 nm, retention time t_{minor} = 8.8 min, t_{major} = 10.2 min. $[\alpha]^{22}_D$ = −36.3° (c = 0.88, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.43 (m, 2H), 7.32 (m, 3H), 4.75 (t, 1H, J = 6.3 Hz), 2.51 (m, 2H), 2.03 (m, 3H), 0.16 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 131.9, 128.7, 128.5, 122.6, 106.3, 89.4, 85.9, 85.6, 62.2, 36.6, 16.2, 0.3. HRMS [ESI(TOF)] for $C_{16}H_{20}ONaSi$ [M + Na$^+$]: m/z calcd for 279.1181, found 279.1186.

*(R)-1-(p-Tolyl)-7-(trimethylsilyl)hepta-1,6-diyn-3-ol ((R)-**1b**).* Light yellow oil, 186.3 mg, 92% yield. 89% ee determined by HPLC analysis: CHIRALPAK AD-H column, 93:7 hexanes: ^{i}PrOH, flow rate 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 5.7 min, t_{major} = 6.9 min. $[\alpha]^{23}_D$ = −37.1° (c = 3.34, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.31 (d, 2H, J=8.1), 7.11 (d, 2H, J = 8.4), 4.74 (t, 1H, J = 6.6 Hz), 2.48 (m, 2H), 2.34 (s, 3H), 2.02 (m, 2H), 0.16 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.9, 131.8, 129.3, 119.6, 106.4, 88.7, 85.8, 85.7, 62.2, 36.7, 21.7, 16.2, 0.3. HRMS [ESI(TOF)] for $C_{17}H_{22}ONaSi$ [M + Na$^+$]: m/z calcd 293.1338, found 293.1352.

*(R)-9-Phenyl-1-(trimethylsilyl)nona-1,6-diyn-5-ol ((R)-**1c**).* Colorless oil, 191.7 mg, 90% yield. 88% ee determined by HPLC analysis: CHIRALPAK AD-H column, 99/1 hexanes/^{i}PrOH, flow rate 1.0 mL/min, λ 254 nm, retention time t_{minor} = 11.8 min, t_{major} = 13.3 min. $[\alpha]^{22}_D$ = −14.7° (c = 3.20, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (m, 5H), 4.48 (m, 1H), 2.82 (m, 2H), 2.51 (m, 2H), 2.35 (m, 2H), 1.85 (m, 3H), 0.15 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7, 128.7, 128.6, 126.6, 106.5, 85.6, 85.5, 81.4, 61.9, 36.8, 35.2, 21.1, 16.1, 0.3. HRMS [ESI(TOF)] for $C_{18}H_{25}OSi$ [M + H$^+$]: m/z calcd 285.1675, found 285.1681.

*(R)-1-(Trimethylsilyl)undeca-1,6-diyn-5-ol ((R)-**1d**).* Light yellow oil, 127.4 mg, 72% yield. 86% ee determined by ^1H and ^{19}F NMR analyses of the corresponding (R)-Mosher ester. $[\alpha]^{22}_D$ = −12.2° (c = 0.64, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.49 (m, 1H), 2.41 (m, 2H), 2.20 (m, 2H), 1.87 (m, 3H), 1.43 (m, 4H), 0.91 (t, 3H, J=7.2 Hz), 0.14 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.5, 86.4, 85.6, 80.5, 62.0, 36.9, 30.9, 22.1, 18.6, 16.2, 13.8, 0.3. HRMS [ESI(TOF)] for $C_{14}H_{25}OSi$ [M + H$^+$]: m/z calcd 237.1675, found 237.1680.

*(R)-1-(Trimethylsilyl)trideca-1,6-diyn-5-ol ((R)-**1e**).* Light yellow oil, 136.6 mg, 69% yield. 86% ee determined by ^1H and ^{19}F NMR analyses of the corresponding (R)-Mosher ester. $[\alpha]^{22}_D$ = −15.3° (c = 0.65, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.49 (m, 1H), 2.39 (m, 2H), 2.19 (m, 2H), 1.95 (s, 1H), 1.87 (m, 2H), 1.49 (m, 2H), 1.37 (m, 2H), 1.28 (m, 4H), 0.88 (t, 3H, J = 6.9 Hz), 0.14 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.5, 86.4, 85.5, 80.6, 62.0, 36.9, 31.5, 28.8, 28.7, 22.8, 18.9, 16.2, 14.3, 0.3. HRMS [ESI(TOF)] for $C_{16}H_{29}OSi$ [M + H$^+$]: m/z calcd 265.1988, found 265.1994.

*(R)-10-Chloro-1-(trimethylsilyl)deca-1,6-diyn-5-ol ((R)-**1f**).* Light yellow oil, 134.4 mg, 70% yield. 88% ee determined by ^1H NMR analyses of the corresponding (R)-Mosher ester. $[\alpha]^{22}_D$ = −15.3° (c = 0.87, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.49 (m, 1H), 3.63 (t, 2H, J = 6.3 Hz), 2.40 (m, 4H), 2.08 (s, 1H), 1,91 (m, 4H), 0.13 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 106.3, 85.7, 84.2, 81.7, 61.9, 43.8, 36.8, 31.4, 16.3, 16.2, 0.3. HRMS [ESI(TOF)] for $C_{13}H_{22}OSiCl$ [M + H$^+$]: m/z calcd 257.1128, found 257.1129.

*(R)-1-Phenoxy-8-(trimethylsilyl)octa-2,7-diyn-4-ol ((R)-**1g**).* Light yellow oil, 152.3 mg, 71% yield. 92% ee determined by ^1H NMR analyses of the corresponding (R)-Mosher ester. $[\alpha]^{22}_D$ = −15.0° (c = 1.07, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (m, 2H), 6.98 (m, 3H), 4.72 (d, 2H, J = 1.5 Hz), 4.56 (m, 1H), 2.34 (m, 3H), 1.90 (q, 2H, J = 6.6 Hz), 0.15 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.8, 129.7, 121.8, 115.1, 106.1, 87.8, 85.9, 80.4, 61.6, 56.2, 36.3, 16.1, 0.3. HRMS [ESI(TOF)] for $C_{17}H_{23}O_2Si$ [M + H$^+$]: m/z calcd 287.1467, found 287.1468.

General Procedure for Preparation of the Unsubstituted Diene-Diynes (*R*)-2a−g. Under nitrogen, KO^{t}Bu (4 equiv) was weighed into a flask and dissolved in THF (10 mL). Then a propargylic alcohol (1 equiv) and 1-bromo-2,4-hexadiene (2 equiv) were added sequentially. The mixture was stirred at room temperature for 15 h. The reaction mixture was quenched with saturated aqueous ammonium chloride and extracted three times with CH_2Cl_2. The organic layer was dried with anhydrous Na_2SO_4 and concentrated by rotary evaporation. The resultant oil was purified by flash column chromatography on silica gel with hexanes/dichloromethane to give the products (R)-**2a**−**g** in 50−86% yield.

Characterization of Compounds (*R*)-2a−g. *((R)-3-((2E,4E)-Hexa-2,4-dien-1-yloxy)hepta-1,6-diyn-1-yl)benzene ((R)-**2a**).* Prepared from (R)-**1a** (184.8 mg, 0.722 mmol), light yellow oil, 123.0 mg, 65% yield. $[\alpha]^{22}_D$ = 95.0° (c = 1.71, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.43 (m, 2H), 7.30 (m, 3H), 6.25 (m, 1H), 6.06 (m, 1H), 5.72 (m, 1H), 5.65 (m, 1H), 4.44 (m, 1H), 4.32 (dd, 1H, J = 12, 6 Hz), 4.05 (dd, 1H, J = 12, 6 Hz), 2.43 (m, 2H), 2.03 (m, 2H), 1.96 (t, 1H, 3 Hz), 1.75 (d, 3H, J = 6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.7, 131.7, 130.8, 130.2, 128.4, 128.3, 126.2, 122.6, 87.5, 86.1, 83.5, 69.3, 68.7, 67.5, 34.6, 18.1, 14.7.

*1-((R)-3-((2E,4E)-Hexa-2,4-dien-1-yloxy)hepta-1,6-diyn-1-yl)-4-methylbenzene ((R)-**2b**).* Prepared from (R)-**1b** (227.7 mg, 0.843 mmol), yellow oil, 125.8 mg, 54% yield. $[\alpha]^{22}_D$ = 95.5° (c = 1.23, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.32 (d, 2H, J=8.4 Hz), 7.10 (d, 2H, 7.8 Hz), 6.25 (m, 1H), 6.06 (m, 1H), 5.72 (m, 1H), 5.65 (m, 1H), 4.43 (t, 1H, J = 6 Hz), 4.31 (dd, 1H, J = 12, 6 Hz), 4.04 (dd, 1H, J = 12, 6.6 Hz), 2.42 (m, 2H), 2.34 (s, 3H), 2.02 (m, 2H), 1.96 (t, 1H, J=2.4 Hz), 1.75 (d, 3H, J=6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 138.5, 133.6, 131.6, 130.8, 130.1, 129.0, 126.2, 119.5, 86.7, 86.2, 83.6, 69.2, 68.7, 67.5, 34.6, 21.5, 18.1, 14.7

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)nona-3,8-diyn-1-yl)benzene ((R)-**2c**).* Prepared from (R)-**1c** (211.5 mg, 0.745 mmol), light yellow oil, 178.8 mg, 82% yield. $[\alpha]^{22}_D$ = 64.7° (c = 0.79, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.29 (m, 2H), 7.22 (m, 3H), 6.17 (m, 1H), 6.04 (m, 1H), 5.71 (m, 1H), 5.59 (m, 1H), 4.17 (m, 2H), 3.89 (m, 1H), 2.82 (t, 2H, J = 7.2 Hz), 2.52 (t, 2H, J = 7.2 Hz), 2.30 (m, 2H), 1.93 (s, 1H), 1.90 (m, 1H), 1.85 (m, 1H), 1.75 (d, 3H, J = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 140.5, 133.4, 130.8, 129.9, 128.4, 128.3, 126.4, 126.3, 85.9, 83.7, 79.2, 68.9, 68.5, 67.2, 35.0, 34.7, 20.8, 18.1, 14.5.

*(R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)undeca-1,6-diyne ((R)-**2d**).* Prepared from (R)-**1d** (50.0 mg, 0.212 mmol), colorless oil, 26.1 mg, 50% yield. $[\alpha]^{21}_D$ = 78.8° (c = 0.53, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.68 (m, 1H), 5.60 (m, 1H), 4.22 (dd, 1H, J = 12.6, 6 Hz), 4.17 (t, 1H, J = 6.6 Hz), 3.94 (dd, 1H, J = 12.6, 6.6 Hz), 2.34 (m, 2H), 2.21 (m, 2H), 1.89 (m, 3H), 1.73 (d, 3H, J = 6.6 Hz), 1.48 (m, 2H), 1.40 (m, 2H), 0.90 (t, 3H, J = 7.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.3, 130.8, 129.9, 126.4, 86.8, 83.7, 78.3, 68.9, 68.4, 67.3, 34.8, 30.7, 21.9, 18.3, 18.0, 14.6, 13.5.

*(R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)trideca-1,6-diyne ((R)-**2e**).* Prepared from (R)-**1e** (95.1 mg, 0.360 mmol), colorless oil, 69.5 mg, 71% yield. $[\alpha]^{21}_D$ = 66.1° (c = 1.47, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.70 (m, 1H), 5.61 (m, 1H), 4.22 (dd, 1H, J = 12, 5.4 Hz), 4.18 (m, 1H), 3.95 (dd, 1H, J = 12.6, 7.2 Hz), 2.34 (m, 2H), 2.20 (m, 2H), 1.89 (m, 3H), 1.74 (d, 3H, J = 6 Hz), 1.49 (m, 2H), 1.37 (m, 2H), 1.28 (m, 4H), 0.88 (t, 3H, J = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.4, 130.8, 129.9, 126.4, 86.9, 83.7, 78.3, 68.9, 68.4, 67.3, 34.8, 31.3, 28.6, 28.5, 22.5, 18.7, 18.1, 14.6, 14.0.

*(R)-10-Chloro-5-((2E,4E)-hexa-2,4-dien-1-yloxy)deca-1,6-diyne ((R)-**2f**).* Prepared from (R)-**1f** (95.0 mg, 0.371 mmol), colorless oil, 73.3 mg, 75% yield. $[\alpha]^{19}_D$ = 63.3° (c = 0.60, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.21 (m, 1H), 6.04 (m, 1H), 5.71 (m, 1H), 5.60 (m, 1H), 4.20 (m, 2H), 3.94 (m, 1H), 3.63 (m, 2H), 2.41 (m, 2H), 2.33 (m, 2H), 1.94 (m, 4H), 1.87 (m, 1H), 1.74 (d, 3H, J = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.5, 130.8, 130.1, 126.2, 84.6, 83.6, 79.5, 69.1, 68.6, 67.2, 43.6, 34.7, 31.3, 18.1, 16.2, 14.6.

*(((R)-4-((2E,4E)-Hexa-2,4-dien-1-yloxy)octa-2,7-diyn-1-yl)oxy)-benzene ((R)-**2g**).* Prepared from (R)-**1g** (112.0 mg, 0.392 mmol),

colorless oil, 99.4 mg, 86% yield. $[\alpha]^{20}_{D}$ = 74.8° (c = 1.75, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.30 (m, 2H), 6.98 (m, 3H), 6.15 (m, 1H), 6.02 (m, 1H), 5.67 (m, 1H), 5.56 (m, 1H), 4.73 (s, 2H), 4.25 (m, 1H), 4.18 (m, 1H), 3.92 (m, 1H), 2.32 (m, 2H), 1.90 (m, 3H), 1.74 (d, 3H, J = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 157.5, 133.8, 130.7, 130.3, 129.4, 125.9, 121.5, 115.0, 85.9, 83.3, 81.0, 69.3, 68.8, 66.8, 56.0, 34.3, 18.1, 14.5.

General Procedure for Preparation of the Optically Active Propargyl 2,4-Hexadienyl Ethers (*R*)-3. Under nitrogen, (*R*)-2 (1 equiv) was dissolved in THF (5 mL) and cooled to −78 °C under nitrogen. ^{n}BuLi (2.5 M in hexane, 1.2 equiv) was added, and the mixture was stirred for 30 min. Then TMSCl or MeI (3 equiv) was added and the system was stirred for 18 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride solution and extracted with CH_2Cl_2 three times. The organic layer was washed with brine, dried with Na_2SO_4, concentrated by rotary evaporation, and purified by column chromatography on silica gel with hexanes/dichloromethane to give the products (*R*)-3 in 70−91% yield.

Characterization of the Optically Active Dienediynes (*R*)-3. *((R)-3-((2E,4E)-Hexa-2,4-dien-1-yloxy)octa-1,6-diyn-1-yl)benzene ((R)-**3**-Me).* Prepared from (*R*)-**2a** (172.0 mg, 0.652 mmol), colorless oil, 144.5 mg, 80% yield. $[\alpha]^{22}_{D}$ = 77.5° (c = 1.30, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.43 (m, 2H), 7.30 (m, 3H), 6.25 (m, 1H), 6.06 (m, 1H), 5.72 (m, 1H), 5.66 (m, 1H), 4.43 (t, 1H, J = 6.6 Hz), 4.32 (dd, 1H, J = 12, 5.4 Hz), 4.05 (dd, 1H, J = 12, 6.6 Hz), 2.35 (m, 2H), 1.97 (m, 2H), 1.77 (s, 3H), 1.75 (d, 3H, J = 6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.6, 131.7, 130.8, 130.1, 128.3, 128.2, 126.3, 122.7, 87.9, 85.9, 78.1, 76.0, 69.2, 67.7, 35.2, 18.1, 15.0, 3.5. HRMS [ESI(TOF)] for $C_{20}H_{23}O$ [M + H^+]: m/z calcd 279.1749, found 279.1749.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)-7-phenylhepta-1,6-diyn-1-yl)trimethylsilane ((R)-**3a**).* Prepared from (*R*)-**2a** (123.0 mg, 0.466 mmol), colorless oil, 127.6 mg, 82% yield. $[\alpha]^{22}_{D}$ = 69.3° (c = 1.92, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.44 (m, 2H), 7.30 (m, 3H), 6.25 (m, 1H), 6.06 (m, 1H), 5.72 (m, 1H), 5.65 (m, 1H), 4.43 (t, 1H, J = 7.2 Hz), 4.31 (dd, 1H, J = 12, 6 Hz), 4.06 (dd, 1H, J = 12, 7.2 Hz), 2.46 (m, 2H), 2.01 (m, 2H), 1.75 (d, 3H, J = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.7, 131.7, 130.8, 130.1, 128.3, 128.2, 126.2, 122.6, 106.3, 87.7, 86.0, 85.0, 69.2, 67.4, 34.8, 18.1, 16.1, 0.1. HRMS [ESI(TOF)] for $C_{22}H_{29}OSi$ [M + H^+]: m/z calcd 337.1988, found 337.1995.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)-7-(p-tolyl)hepta-1,6-diyn-1-yl)trimethylsilane ((R)-**3b**).* Prepared from (*R*)-**2b** (125.8 mg, 0.453 mmol), colorless oil, 111.2 mg, 70% yield. $[\alpha]^{22}_{D}$ = 63.6° (c = 1.89, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.32 (d, 2H, J = 8.4 Hz), 7.10 (d, 2H, 7.8 Hz), 6.25 (m, 1H), 6.06 (m, 1H), 5.72 (m, 1H), 5.65 (m, 1H), 4.42 (m, 1H), 4.31 (dd, 1H, J = 12.6, 6 Hz), 4.05 (dd, 1H, J = 12, 6.6 Hz), 2.46 (m, 2H), 2.34 (s, 3H), 2.00 (m, 2H), 1.75 (d, 3H, J = 6 Hz), 0.15 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 138.4, 133.6, 131.6, 130.9, 130.1, 129.0, 126.3, 119.6, 106.3, 86.9, 86.1, 84.9, 69.2, 67.5, 34.8, 21.5, 18.1, 16.1, 0.1. HRMS [ESI(TOF)] for $C_{23}H_{31}OSi$ [M + H^+]: m/z calcd 351.2144, found 351.2141.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)-9-phenylnona-1,6-diyn-1-yl)trimethylsilane ((R)-**3c**).* Prepared from (*R*)-**2c** (178.8 mg, 0.612 mmol), colorless oil, 203.8 mg, 91% yield. $[\alpha]^{22}_{D}$ = 45.7° (c = 1.02, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.29 (m, 2H), 7.21 (m, 3H), 6.17 (m, 1H), 6.04 (m, 1H), 5.69 (m, 1H), 5.58 (m, 1H), 4.15 (m, 2H), 3.89 (dd, 1H, J = 12.6, 7.2 Hz), 2.82 (t, 2H, J = 7.2 Hz), 2.52 (t, 2H, J = 7.2 Hz), 2.33 (m, 2H), 1.86 (m, 2H), 1.75 (d, 3H, J = 6.6 Hz), 0.14 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 140.5, 133.4, 130.9, 129.9, 128.4, 128.3, 126.4, 126.3, 106.5, 85.7, 84.7, 79.4, 68.8, 67.1, 35.0, 34.9, 20.9, 18.0, 16.0, 0.1. HRMS [ESI(TOF)] for $C_{24}H_{33}OSi$ [M + H^+]: m/z calcd 365.2301, found 365.2298.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)undeca-1,6-diyn-1-yl)-trimethylsilane ((R)-**3d**).* Prepared from (*R*)-**2d** (26.1 mg, 0.091 mmol), colorless oil, 29.1 mg, 86% yield. $[\alpha]^{20}_{D}$ = 48.3° (c = 1.46, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.69 (m, 1H), 5.60 (m, 1H), 4.21 (dd, 1H, J = 12.6, 6 Hz), 4.16 (t, 1H, J = 6 Hz), 3.95 (dd, 1H, J = 12.6, 6.6 Hz), 2.36 (m, 2H), 2.20 (t, 2H, J = 5.4 Hz), 1.87 (m, 2H), 1.73 (d, 3H, J = 6.6 Hz), 1.48 (m, 2H), 1.40 (m, 2H), 0.90 (t, 3H, J = 7.2 Hz), 0.12 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.4, 130.9, 129.9, 126.4, 106.5, 86.6, 84.7, 78.4, 68.8, 67.2, 35.0, 30.7, 21.9, 18.4, 18.1, 16.0, 13.6, 0.1. HRMS [ESI(TOF)] for $C_{20}H_{33}OSi$ [M + H^+]: m/z calcd 317.2301, found 317.2298.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)trideca-1,6-diyn-1-yl)-trimethylsilane ((R)-**3e**).* Prepared from (*R*)-**2e** (69.5 mg, 0.256 mmol), colorless oil, 66.6 mg, 76% yield. $[\alpha]^{20}_{D}$ = 48.0° (c = 1.65, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.69 (m, 1H), 5.60 (m, 1H), 4.20 (dd, 1H, J = 12, 5.4 Hz), 4.16 (t, 1H, J = 6 Hz), 3.95 (m, 1H, J = 12.6, 6.6 Hz), 2.37 (m, 2H), 2.20 (t, 2H, J = 6 Hz), 1.88 (m, 2H), 1.73 (d, 3H, J = 6.6 Hz), 1.49 (m, 2H), 1.37 (m, 2H), 1.28 (m, 4H), 0.88 (t, 3H, J = 6.6 Hz), 0.13 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.4, 130.9, 129.9, 126.4, 106.5, 86.7, 84.7, 78.4, 68.8, 67.2, 35.0, 31.3, 28.6, 28.5, 22.5, 18.7, 18.1, 16.0, 14.0, 0.1. HRMS [ESI(TOF)] for $C_{22}H_{37}OSi$ [M + H^+]: m/z calcd 345.2614, found 345.2619.

*((R)-10-Chloro-5-((2E,4E)-hexa-2,4-dien-1-yloxy)deca-1,6-diyn-1-yl)trimethylsilane ((R)-**3f**).* Prepared from (*R*)-**2f** (31.5 mg, 0.119 mmol), colorless oil, 30.3 mg, 76% yield. $[\alpha]^{20}_{D}$ = 48.1° (c = 1.52, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.70 (m, 1H), 5.59 (m, 1H), 4.20 (m, 1H), 4.16 (m, 1H), 3.95 (m, 1H), 3.63 (t, 2H, J = 6.6 Hz), 2.41 (m, 2H), 2.35 (m, 2H), 1.95 (t, 2H, J = 6.6 Hz), 1.87 (m, 2H), 1.74 (d, 3H, J = 6.6 Hz), 0.13 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 133.5, 130.8, 130.1, 126.2, 106.3, 84.9, 84.4, 79.7, 69.0, 67.1, 43.6, 34.9, 31.3, 18.1, 16.2, 16.0, 0.1. HRMS [ESI(TOF)] for $C_{19}H_{30}OSiCl$ [M + H^+]: m/z calcd 337.1754, found 337.1762.

*((R)-5-((2E,4E)-Hexa-2,4-dien-1-yloxy)-8-phenoxyocta-1,6-diyn-1-yl)trimethylsilane ((R)-**3g**).* Prepared from (*R*)-**2g** (99.4 mg, 0.338 mmol), colorless oil, 94.6 mg, 76% yield. $[\alpha]^{20}_{D}$ = 57.8° (c = 0.78, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ 7.30 (t, 2H, J = 7.2 Hz), 6.98 (m, 3H), 6.13 (m, 1H), 6.01 (m, 1H), 5.68 (m, 1H), 5.56 (m, 1H), 4.73 (s, 2H), 4.23 (t, 1H, J = 6 Hz), 4.17 (dd, 1H, J = 12.6, 6 Hz), 3.92 (dd, 1H, J = 12, 7.2 Hz), 2.35 (m, 2H), 1.89 (m, 2H), 1.73 (d, 3H, J = 6.6 Hz), 0.13 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 157.5, 133.8, 130.7, 130.2, 129.4, 125.9, 121.4, 115.0, 106.0, 86.0, 85.1, 80.8, 69.2, 66.8, 56.0, 34.4, 18.1, 15.9, 0.1. HRMS [ESI(TOF)] for $C_{23}H_{31}O_2Si$ [M + H^+]: m/z calcd 367.2093, found 367.2099.

General Procedure for the Catalytic Domino PK/DA Cycloaddition. Under nitrogen, a propargyl 2,4-hexadienyl ether (1 equiv) and $[Rh(CO)_2Cl]_2$ (0.1 equiv) were weighed into a tared two-necked round-bottom flask and dissolved in 1,2-dichloroethane (DCE, 5 mL). The flask was fitted with a reflux condenser equipped with a septum, and the side arm of the flask was also equipped with a septum. The solution was bubbled with CO gas for 2 min through the side arm equipped with a septum and a vent needle in the septum of the reflux condenser in a well-vented fume hood. Then, the solution was placed under a CO atmosphere by using a balloon. After the reaction mixture was heated at 80 °C to reflux temperature for 19−26 h, it was cooled to room temperature and the CO was released cautiously in the fume hood. The reaction mixture was concentrated, and the crude product was purified by column chromatography on silica gel with hexanes/ethyl acetate to give the tetracyclic products **4** with 42−64% yield and 87−88% ee.

Characterization of the Domino PK/DA Cycloaddition Products 4. *Compound **4a**.* Prepared from (*R*)-**3a** (127.6 mg, 0.380 mmol), colorless oil, 88.7 mg, 64% yield. 87% ee determined by HPLC analysis: CHIRALPAK AD-H column, 100/0.5 hexanes/^{i}PrOH, flow rate 1.0 mL/min, λ 254 nm, retention time t_{major} = 7.6 min, t_{minor} = 9.4 min. $[\alpha]^{22}_{D}$ = 371.3° (c = 1.18, $CHCl_3$). ^1H NMR (800 MHz, $CDCl_3$): δ 7.27 (m, 2H), 7.19 (m, 1H), 7.02 (br, 2H), 5.88 (m, 1H), 5.84 (m, 1H), 4.16 (t, 1H, J = 7.2 Hz), 3.75 (dd, 1H, J = 12.8, 8 Hz), 3.61 (d, 1H, J = 3.2 Hz), 3.11 (m, 1H), 2.99 (m, 1H), 2.59 (m, 1H), 2.52 (m, 1H), 2.08 (dd, 1H, J = 12.8, 7.2 Hz), 1.26 (d, 3H, J = 7.2 Hz), 1.07 (m, 1H), 0.25 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 211.5, 192.6, 143.7, 139.7, 136.4, 128.5, 127.0, 126.5, 124.5, 80.9, 74.2, 69.7, 65.6, 51.5, 39.8, 37.9, 32.0, 15.3, 0.9. HRMS [ESI(TOF)] for $C_{23}H_{29}O_2Si$ [M + H^+]: m/z calcd 365.1937, found 365.1939.

*Compound **4c**.* Prepared from (*R*)-**3c** (203.8 mg, 0.560 mmol), colorless oil, 131.7 mg, 60% yield. 88% ee determined by HPLC analysis: CHIRALPAK AD-H column, 100/0.5 hexanes/^{i}PrOH, flow rate 1.0 mL/min, λ 254 nm, retention time t_{major} = 8.9 min, t_{minor} = 10.9 min. $[\alpha]^{22}_D$ = 147.4° (c = 0.58, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.27 (m, 2H), 7.18 (m, 3H), 5.82 (m, 1H), 5.66 (m, 1H), 4.69 (d, 1H, J = 4.2 Hz), 4.17 (t, 1H, J = 7.8 Hz), 3.84 (dd, 1H, J = 12.6, 7.8 Hz), 2.90 (m, 1H), 2.64 (dd, 1H, J = 13.8, 7.2 Hz), 2.56 (m, 3H), 2.42 (dd, 1H, J = 13.2, 7.2 Hz), 2.34 (m, 1H), 2.09 (m, 1H), 1.70 (m, 2H), 1.37 (d, 3H, J = 7.2 Hz), 0.16 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 211.1, 192.0, 142.5, 142.1, 136.2, 128.7, 128.3, 126.2, 124.7, 79.9, 71.6, 69.6, 58.8, 52.2, 39.6, 38.7, 33.5, 32.2, 31.0, 15.3, −0.8. HRMS [ESI(TOF)] for $C_{25}H_{33}O_2Si$ [M + H$^+$]: m/z calcd 393.2250, found 393.2250.

*Compound **4-Me**.* Prepared from (R)-**3-Me** (144.5 mg, 0.520 mmol), light yellow oil, 82.7 mg, 52% yield. $[\alpha]^{22}_D$ = 328.8° (c = 1.14, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.27 (m, 3H), 7.03 (m, 2H), 5.89 (m, 1H), 5.83 (m, 1H), 4.17 (t, 1H, J = 7.8 Hz), 3.75 (dd, 1H, J = 12, 7.8 Hz), 3.59 (d, 1H, J = 3 Hz), 3.11 (m, 1H), 3.03 (m, 1H), 2.56 (dd, 1H, J = 20.4, 7.2 Hz), 2.43 (m, 1H), 2.07 (dd, 1H, J = 13.2, 7.2 Hz), 1.82 (s, 3H), 1.27 (d, 3H, J = 7.2 Hz), 1.08 (m, 1H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 208.1, 178.4, 139.6, 139.1, 136.3, 128.7, 127.2, 126.8, 125.2, 81.2, 71.6, 69.9, 64.7, 51.3, 40.2, 38.2, 29.8, 15.4, 9.5. HRMS [ESI(TOF)] for $C_{21}H_{23}O_2$ [M + H$^+$]: m/z calcd 307.1698, found 307.1693.

*Compound **4b**.* Prepared from (R)-**3b** (111.2 mg, 0.318 mmol), colorless oil, 63.2 mg, 53% yield. $[\alpha]^{22}_D$ = 370.6° (c = 1.17, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.07 (d, 2H, J = 7.2 Hz), 6.89 (s, 2H), 5.86 (m, 1H), 5.83 (m, 1H), 4.15 (t, 1H, J=7.2 Hz), 3.74 (m, 1H), 3.64 (s, 1H), 3.09 (m, 1H), 2.95 (s, 1H), 2.58 (m, 1H), 2.52 (m, 1H), 2.28 (s, 3H), 2.08 (m, 1H), 1.25 (d, 3H, J = 6 Hz), 1.07 (m, 1H), 0.24 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 211.6, 192.5, 143.6, 136.6, 136.5, 136.0, 129.2, 126.9, 124.4, 81.0, 74.1, 69.7, 65.3, 51.5, 39.8, 37.9, 32.0, 20.9, 15.3, −0.9. HRMS [ESI(TOF)] for $C_{24}H_{31}O_2Si$ [M + H$^+$]: m/z calcd 379.2093, found 379.2091.

*Compound **4d**.* Prepared from (R)-**3d** (29.1 mg, 0.092 mmol), light yellow oil, 14.1 mg, 45% yield. $[\alpha]^{21}_D$ = 101.3° (c = 0.51, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 5.77 (m, 1H), 5.62 (m, 1H), 4.48 (d, 1H, J = 4.2 Hz), 4.12 (t, 1H, J = 7.8 Hz), 3.79 (dd, 1H, J = 12.6, 7.8 Hz), 2.82 (m, 1H), 2.60 (dd, 1H, J = 13.8, 7.2 Hz), 2.51 (m, 1H), 2.36 (dd, 1H, J = 13.2, 7.2 Hz), 2.27 (m, 1H), 1.79 (m, 1H), 1.63 (m, 1H), 1.29 (d, 3H, J = 7.2 Hz), 1.27 (m, 5H), 0.89 (t, 1H, J = 6.6 Hz), 0.15 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 211.5, 191.7, 142.1, 136.1, 124.3, 79.6, 71.4, 69.4, 58.6, 52.0, 39.3, 38.2, 31.9, 30.8, 26.5, 23.5, 15.0, 13.9, −1.0. HRMS [ESI(TOF)] for $C_{21}H_{33}O_2Si$ [M + H$^+$]: m/z calcd 345.2250, found 345.2245.

*Compound **4e**.* Prepared from (R)-**3e** (26.7 mg, 0.078 mmol), light yellow oil, 16.6 mg, 57% yield. $[\alpha]^{21}_D$ = 134.7° (c = 0.83, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 5.77 (m, 1H), 5.62 (m, 1H), 4.47 (d, 1H, J = 4.2 Hz), 4.12 (t, 1H, J = 7.8 Hz), 3.79 (dd, 1H, J = 12.6, 7.8 Hz), 2.82 (m, 1H), 2.60 (dd, 1H, J = 13.8, 6.6 Hz), 2.52 (m, 1H), 2.36 (dd, 1H, J = 13.2, 7.2 Hz), 2.26 (m, 1H), 1.78 (m, 1H), 1.64 (m, 1H), 1.30 (d, 3H, J = 7.8 Hz), 1.25 (m, 9H), 0.87 (t, 3H, J = 6 Hz), 0.15 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 211.7, 191.9, 142.3, 136.4, 124.5, 79.9, 71.7, 69.6, 58.9, 52.2, 39.5, 38.5, 32.1, 31.8, 31.3, 30.3, 24.6, 22.8, 15.2, 14.2, −0.7. HRMS [ESI(TOF)] for $C_{23}H_{37}O_2Si$ [M + H$^+$]: m/z calcd 373.2563, found 373.2561.

*Compound **4f**.* Prepared from (R)-**3f** (30.3 mg, 0.090 mmol), colorless oil, 16.4 mg, 50% yield. $[\alpha]^{21}_D$ = 182.0° (c = 0.35, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 5.78 (m, 1H), 5.62 (m, 1H), 4.55 (d, 1H, J = 3 Hz), 4.12 (t, 1H, J = 7.2 Hz), 3.79 (dd, 1H, J = 13.2, 9 Hz), 3.50 (m, 2H), 2.79 (m, 1H), 2.61 (dd, 1H, J = 13.8, 7.2 Hz), 2.51 (m, 1H), 2.37 (dd, 1H, J = 13.2, 7.2 Hz), 2.22 (m, 1H), 1.91 (m, 1H), 1.72 (m, 2H), 1.65 (m, 1H), 1.57 (m, 1H), 1.29 (d, 3H, J = 7.2 Hz), 0.15 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 210.7, 191.9, 142.2, 135.8, 124.6, 79.4, 71.3, 69.3, 57.9, 51.9, 45.3, 39.3, 38.5, 31.9, 28.3, 27.6, 15.0,-1.0. HRMS [ESI(TOF)] for $C_{20}H_{30}O_2SiCl$ [M + H$^+$]: m/z calcd 365.1704, found 365.1704.

*Compound **4g**.* Prepared from (R)-**3g** (94.6 mg, 0.258 mmol), light yellow oil, 42.8 mg, 42% yield. $[\alpha]^{21}_D$ = 190.4° (c = 0.66, CHCl$_3$). ^{1}H NMR (600 MHz, CDCl$_3$): δ 7.24 (t, 2H, J = 7.2 Hz), 6.92 (t, 1H, J = 7.8 Hz), 6.80 (d, 1H, J = 8.4 Hz), 5.85 (m, 1H), 5.66 (m, 1H), 4.51 (s, 1H), 4.15 (dd, 2H, J = 15.6, 7.2 Hz), 4.08 (d, 1H, J = 9 Hz), 3.81 (dd, 1H, J = 12.6, 8.4 Hz), 2.97 (m, 1H), 2.66 (dd, 1H, J = 13.8, 6.6 Hz), 2.58 (m, 1H), 2.52 (m, 1H), 2.32 (dd, 1H, J = 12.6, 7.2 Hz), 1.75 (m, 1H), 1.37 (d, 3H, J = 6.6 Hz), 0.18 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 208.7, 193.1, 158.3, 142.8, 135.6, 129.4, 124.9, 121,1, 114.3, 79.9, 70.4, 69.3, 67.7, 59.5, 51.5, 39.0, 36.8, 32.2, 15.1, −1.0. HRMS [ESI(TOF)] for $C_{24}H_{31}O_3Si$ [M + H$^+$]: m/z calcd 395.2042, found 395.2039.

Characterization of Additional Dienediyne Substrates and a PK Product. *6-((2E,4E)-Hexa-2,4-dien-1-yloxy)dodeca-2,7-diyne (**3i**).* Colorless oil, 72 mg, 74% yield. ^{1}H NMR (600 MHz, CDCl$_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.69 (m, 1H), 5.61 (m, 1H), 4.22 (dd, 1H, J = 12, 5.4 Hz), 4.16 (t, 1H, J=6 Hz), 3.95 (dd, 1H, J=12.6, 7.2 Hz), 2.27 (m, 2H), 2.20 (t, 2H, J = 7.2 Hz), 1.86 (m, 1H), 1.80 (m, 1H), 1.75 (s, 3H), 1.73 (d, 3H, J = 7.2 Hz), 1.48 (m, 2H), 1.40 (m, 2H), 0.90 (t, 3H, J = 7.8 Hz). ^{13}C NMR (150 MHz, CDCl$_3$): δ 133.2, 130.9, 129.8, 126.6, 86.5, 78.6, 78.3, 75.7, 68.8, 67.5, 35.4, 30.8, 21.9, 18.4, 18.0, 14.9, 13.5, 3.4. HRMS [ESI(TOF)] for $C_{18}H_{27}O$ [M + H$^+$]: m/z calcd 259.2062, found 259.2064.

*(3-((2E,4E)-Hexa-2,4-dien-1-yloxy)hepta-1,6-diyne-1,7-diyl)bis(trimethylsilane) (**3j**).* Colorless oil, 120.2 mg, 87% yield. ^{1}H NMR (600 MHz, CDCl$_3$): δ 6.20 (m, 1H), 6.04 (m, 1H), 5.70 (m, 1H), 5.60 (m, 1H), 4.22 (dd, 1H, J = 12, 5.4 Hz), 4.17 (t, 1H, J = 7.2 Hz), 3.96 (dd, 1H, J = 12.6, 7.2 Hz), 2.37 (m, 2H), 1.90 (m, 2H), 1.74 (d, 3H, J = 6.6 Hz), 0.16 (s, 9H), 0.13 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 133.6, 130.8, 130.0, 126.2, 106.3, 104.1, 90.7, 84.8, 69.0, 67.3, 34.6, 18.0, 15.9, 0.09, −0.10. HRMS [ESI(TOF)] for $C_{19}H_{33}OSi_2$ [M + H$^+$]: m/z calcd 333.2070, found 333.2069.

*PK Product **4j**.* light yellow oil, 58.7 mg, 51% yield. ^{1}H NMR (600 MHz, CDCl$_3$): δ 5.56 (m, 2H), 5.00 (d, 1H, J = 10.2 Hz), 4.24 (t, 1H, J = 8.4 Hz), 3.29 (m, 1H), 3.15 (m, 1H), 2.79 (d, 1H, J=5.4 Hz), 2.46 (m, 2H), 1.79 (m, 1H), 1.72 (d, 3H, J=6 Hz), 1.63 (m, 1H), 0.24 (s, 9H), 0.13 (s, 9H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 211.7, 193.3, 134.1, 129.2, 126.6, 105.4, 86.1, 75.1, 68.3, 56.3, 55.1, 33.2, 18.1, 17.2, 0.03, −0.77. HRMS [ESI(TOF)] for $C_{20}H_{33}O_2Si_2$ [M + H$^+$]: m/z calcd 361.2019, found 361.2021.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, tables, and a CIF file giving additional data for synthesis and characterization of the compounds, HPLC plots, NMR spectra, calculated Cartesian coordinates, and X-ray analysis data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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