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Preparation of C_2-Symmetric Allenes by Palladium-Catalyzed Double-Nucleophilic Substitution on 3-Bromopenta-2,4-dienyl Acetate

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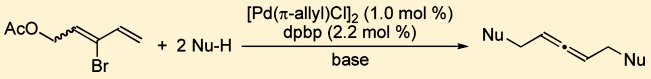
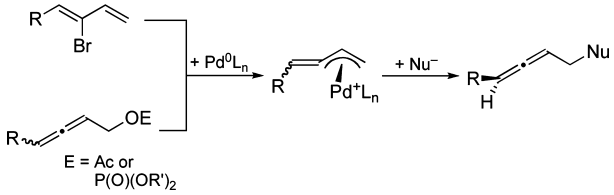
Supporting Information

ABSTRACT: Easily accessible 3-bromopenta-2,4-dienyl acetate was applied to the palladium-catalyzed reaction with soft nucleophiles. The reaction proceeded through the stepwise 2-fold nucleophilic substitution via formal S_N2' and S_N2 processes giving the various doubly functionalized C_2-symmetric allenes in good yields.



Allenes have gained increasing attraction as unique building blocks in synthetic organic chemistry.[1−4] Recently, we developed a palladium-catalyzed reaction for preparing various functionalized allenes starting with easily accessible 1-hydrocarbyl-2-bromo-1,3-dienes (Scheme 1, top).[5−8] The reaction

Scheme 1. Pd-Catalyzed Nucleophilic Substitution on 2-Bromo-1,3-dienes and Allenylmethyl Esters

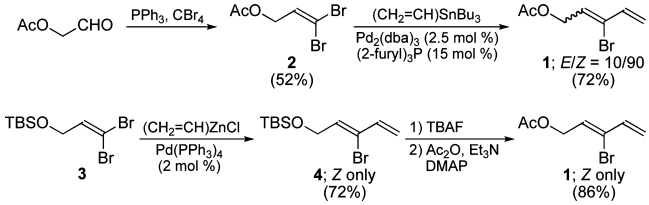


has been extended to the asymmetric counterparts using an appropriate chiral palladium catalyst to give the corresponding axially chiral allenes of high enantiopurity.[9−12] The reaction proceeds via an (alkylidene-π-allyl)palladium intermediate[13,14] that is somewhat similar to the widely accepted intermediates in the Tsuji−Trost reaction.[15−18] Alternatively, an analogous (alkylidene-π-allyl)palladium species can be generated by oxidative addition of an allenylmethyl ester to a zerovalent palladium species,[19−23] and its reaction with appropriate nucleophiles also provides comparable allenic products (Scheme 1, bottom).[24−27] Since an allenic C=C=C moiety preexists in the allenylmethyl esters, their palladium-catalyzed nucleophilic substitution is better described as "functionalization of allenes" rather than "preparation of allenes". Nevertheless, the two Pd-catalyzed processes shown in Scheme 1 are closely related to each other.

In the course of our studies on the Pd-catalyzed reaction of the bromodienes,[5−13] we were interested in examining the reactivity of 3-bromopenta-2,4-dienyl acetate (**1**). Compound **1** is a bifunctional molecule and possesses properties and substructures of both 2-bromo-1,3-dienes and allylic acetates. Indeed, **1** undergoes the facile 2-fold Pd-catalyzed nucleophilic substitution, once via a formal S_N2'-substition as with our allene synthesis reaction and the other via a formal S_N2-substitution as with the Tsuji−Trost reaction, to afford various doubly functionalized C_2-symmetric allenes in high yields with excellent regioselectivity. Here we report details of this palladium-catalyzed double nucleophilic substitution process.

Preparation of 3-Bromopenta-2,4-dienyl Acetate (1). The substrate for this study, 3-bromopenta-2,4-dienyl acetate (**1**), was prepared by two routes as shown in Scheme 2.[28,29]

Scheme 2. Preparation of 3-Bromopenta-2,4-dienyl Acetate (1)



The Pd-catalyzed Stille coupling of 3,3-dibromo-2-propenyl acetate (**2**), which was obtained by the Wittig dibromoolefination of formylmethyl acetate,[30,31] with tributylvinyltin gave **1** in 72% yield as an inseparable mixture of the *E*- and *Z*-isomers (*E*/*Z* = 10/90 determined by ^{1}H NMR; Scheme 2 top).[32−34] The identity of the minor isomer in **1** ((*E*)-isomer) was confirmed by GC−MS and ^{1}H NMR analyses. On the other hand, the Pd-catalyzed Negishi coupling of TBS-protected 3,3-dibromo-2-propenol **3** with vinylzinc chloride proceeded with excellent regioselectivity to give (*Z*)-bromo-diene **4** in 72% yield exclusively.[5,28,29,35−40] Deprotection of **4** followed by acetylation afforded (*Z*)-**1** in 86% yield in isomerically pure form.

Palladium-Catalyzed Nucleophilic Substitution of 1. Substrate **1** was subjected to the Pd-catalyzed reaction with various soft nucleophiles generated from **5a−g** and an

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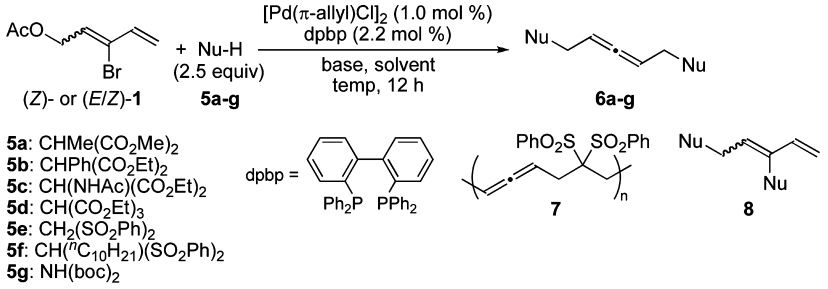
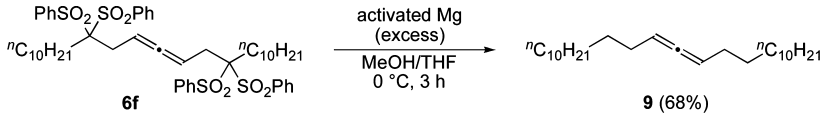
Table 1. Palladium-Catalyzed Synthesis of C_2-Symmetric Allenes 6[a]



entry	substrate 1	Nu-H 5	base	solvent	temp (°C)	yield of 6[b] (%)
1	(Z)-1	5a	NaH	THF	40	83 (6a)
2	(E/Z)-1	5a	NaH	THF	40	87 (6a)
3	(E/Z)-1	5b	^{t}BuOK	THF	40	84 (6b)
4	(Z)-1	5c	^{t}BuOK	CH_2Cl_2	23	73 (6c)
5	(Z)-1	5d	^{t}BuOK	THF	23	81 (6d)
6	(E/Z)-1	5e	NaH	THF	40	46 (6e)
7	(E/Z)-1	5f	NaH	THF	40	89 (6f)
8	(Z)-1	5g	^{t}BuOK	THF	23	67 (6g)

[a]The reaction was carried out with **1** (0.50 mmol) and **5** (1.25 mmol) in the given solvent in the presence of an appropriate base and a Pd catalyst (2 mol %) generated from $[PdCl(\pi\text{-allyl})]_2$ and dpbp. [b]Isolated yield by silica gel chromatography.

Scheme 3. Preparation of Allenic Hydrocarbon 9 by Reductive Desulfonylation of 6f



appropriate base (Table 1). The Pd-catalyzed reaction of (*Z*)-**1** with **5a** (2.5 equiv with respect to **1**) gave allene **6a** in 83% yield (entry 1). Similarly, the *E*/*Z* mixture of **1** afforded **6a** in 87% yield under the identical conditions (entry 2). These results are consistent with our previous reports, which describes analogous reactivity between (*E*)- and (*Z*)-isomers of 1-substituted-2-bromo-1,3-dienes in the Pd-catalyzed reaction.[6,13] During the transformation of **1** into **6**, the *E*/*Z* isomeric difference in **1** is canceled due to the perpendicular structure of the allenic C═C═C moiety in **6**, and the isostructural allene is obtained from either (*E*)- or (*Z*)-**1**. Thus, the *E*/*Z* mixture of **1** can be used for the allene synthesis without separating the two isomers. Under similar conditions, the reactions of phenylmalonate **5b** (with (*E*/*Z*)-**1**) or acetamidemalonate **5c** (with (*Z*)-**1**) provided the corresponding doubly functionalized allenes **6b** or **6c** in 84% or 73% yields, respectively (entries 3 and 4). Triethyl methanetricarboxylate **5d** was also a reactive pronucleophile to give allene **6d** in 81% yield from (*Z*)-**1** in the same way (entry 5). The *gem*-bis(phenylsulfonyl)alkanes such as **5e** and **5f** could be used as pronucleophiles in the present transformation,[41] and the corresponding C_2-symmetric allenes **6e** and **6f** were obtained from (*E*/*Z*)-**1**, respectively (entries 6 and 7). The yield of **6e** is relatively low (46%), although substrate **1** was completely consumed under the conditions shown in Table 1 (entry 6). Pronucleophile **5e** possesses two active methylene hydrogen atoms, and it is capable of reacting with 2-fold **1**. Thus, the formation of oligomeric allenes **7**, presumably, competed to a certain extent lowering the yield of monomeric **6e**. Indeed, the reaction using **5f**, which has only one acidic methine hydrogen atom, gave the corresponding C_2-symmetric allene (**6f**) in much higher yield of 89% (entry 7). This synthetic protocol was applicable to the reaction with *N*-pronucleophile **5g** as well, and diaminoallene derivative **6g** was isolated in 67% yield by the reaction between (*Z*)-**1** and **5g** (entry 8). The present reaction is highly regioselective. Except for the formation of **7**, the doubly substituted products are allenes **6** exclusively, and regioisomers such as **8** were not detected in any cases.

The phenylsulfonyl groups in **6f** could be removed by a treatment with activated magnesium in MeOH/THF according to the Carpino's procedure[42,43] to give allenic hydrocarbon **9** in 68% yield (Scheme 3). This process can be an efficient method for preparing symmetric allenic hydrocarbons. Indeed, practical applicability of the sequential processes was demonstrated by the experiments on a semimacro scale: 403 mg (1.97 mmol) of **1** afforded 1.68 g (1.79 mmol) of **6f** (91% yield), which could be converted to **9** (451 mg) in 67% yield.

The C_2-symmetric allenes **6** are axially chiral, and application of an appropriate chiral palladium species to the reaction may furnish allenes **6** in enantiomerically enriched forms.[3,9−12] The asymmetric extension was explored for a reaction of **1** with **5c**, and the results are shown in Scheme 4. The asymmetric reaction catalyzed by a palladium species generated from $Pd(dba)_2$ and (*R*)-segphos[44] proceeded with excellent enantioselectivity at 23 °C, and (−)-**6c** of 96% ee was obtained in 44% yield using CsO^{t}Bu as a base.[9] The yield of (−)-**6c** could be increased to 70% at 40 °C; however, the enantioselectivity was diminished to 81% ee. The absolute configuration of levorotatory (−)-**6c** was deduced to be (*R*) by the Lowe−Brewster rule.[45,46]

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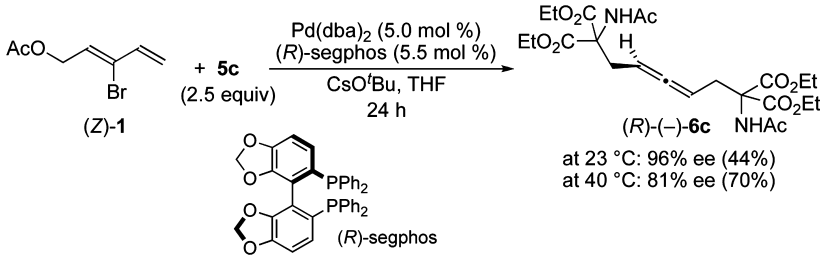
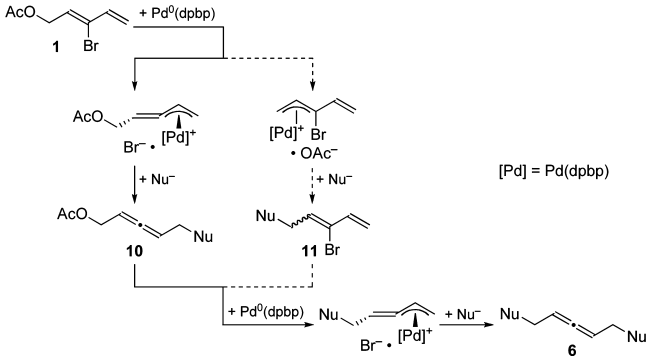
Scheme 4. Palladium-Catalyzed Asymmetric Synthesis of Axially Chiral Allene (*R*)-(−)-6c



Consideration to Reaction Pathways from 1 to 6. Substrate **1** possesses two different sites susceptible to activation with palladium catalysis, and thus, there are two possible reaction pathways from **1** to **6** (Scheme 5). Treatment

Scheme 5. Possible Reaction Pathways from 1 to 6



of **1** with an equimolar mixture of **5a** and NaH (1 equiv with respect to **1**) in THF in the presence of the Pd/dpbp catalyst (2 mol %) did not afford either **10** or **11**, but the reaction mixture contained unreacted **1** and **6a** both in ca. 50% yields. Apparently, monosubstituted intermediates **10** and/or **11** are more reactive than **1** under the present reaction conditions.

Pd-catalyzed reactions of compounds having an 1-acetoxy-3-bromo-2-propene substructure, which is a substructure shown in **1**, were examined by de Meijere[47] and Organ.[48] They showed that the vinylic bromo substituents deactivated the allylic acetate moieties toward ionization in the presence of the Pd catalyst. Thus, oxidative addition of Pd(0) to the vinylic C−Br takes place preferentially to ionization at the allylic acetate. Because of the close structural similarity between their substrates and **1**, we propose that the route via **10** is the most likely pathway from **1** to **6** in the present reaction. The deactivating group (vinylic Br) is eliminated during the first Pd-catalyzed process, and thus, monosubstituted intermediate **10** reacts faster than **1** to furnish **6** even in the presence of remaining **1**. Although this explanation is consistent with the experimental observations, a possibility involving the both pathways cannot be ruled out assuming that both **10** and **11** are more reactive than **1** under the Pd catalysis.

In summary, we have demonstrated that 3-bromopenta-2,4-dienyl acetate **1** is an excellent precursor to a variety of doubly functionalized C_2-symmetric allenes. The reaction is effectively catalyzed by the Pd/dpbp complex, and **1** undergoes the 2-fold nucleophilic substitution via formal S_N2' and S_N2 processes to give the allenic products in high yields.

EXPERIMENTAL SECTION

General Methods. All anaerobic and/or moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or with glovebox techniques under prepurified argon. ^{1}H NMR (at 400 MHz) and ^{13}C NMR (at 101 MHz) chemical shifts are reported in ppm downfield of internal tetramethylsilane. ^{31}P NMR (at 162 MHz) chemical shifts are externally referenced to 85% H_3PO_4. Tetrahydrofuran and benzene were distilled from benzophenone−ketyl under nitrogen prior to use. Dichloromethane was distilled from CaH_2 under nitrogen prior to use. Acetoxyacetaldehyde,[49] (*Z*)-TBS-protected diene **4**,[28] dpbp,[50] and (*R*)-segphos[44] were prepared as reported. All other chemicals were obtained from commercial sources and used without additional purification.

3,3-Dibromo-2-propenyl Acetate (2). This compound was prepared by the reported method with minor modifications. To a CH_2Cl_2 (250 mL) solution of CBr_4 (35.2 g, 106 mmol) was added PPh_3 (55.7 g, 212 mmol) portionwise at 0 °C, and the solution was allowed to stir at this temperature for 30 min. Acetoxyacetaldehyde (5.42 g, 53.1 mmol) was added to the solution at 0 °C, and the mixture was stirred at the same temperature for 30 min. After the reaction mixture was quenched with a small amount of water (ca. 2 mL), the mixture was concentrated under reduced pressure. Addition of hexane (ca. 500 mL) to the concentrated solution precipitated triphenylphosphine oxide as pale yellow solid, which was removed by filtration. The filtrate was evaporated, and the residual oil was purified by column chromatography on silica gel (with hexane/ethyl acetate = 5/1) followed by vacuum transfer to give the title compound (7.16 g, 52% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 2.08 (s, 3 H), 4.56 (d, J = 6.3 Hz, 2H), 6.61 (t, J = 6.3 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 20.7, 63.8, 94.1, 132.7, 170.6. EI-HRMS: calcd for $C_5H_6Br_2O_2$ 255.8735, found 255.8738.

3-Bromo-2,4-pentadienyl Acetate (1). To a toluene (125 mL) solution of $Pd_2(dba)_3{\cdot}CHCl_3$ (325 mg, 0.63 mmol), tri-2-furylphosphine (874 mg, 3.76 mmol), and ^{n}Bu$_3$Sn(vinyl) (7.99 g, 25.1 mmol) was added **2** (6.48 g, 25.1 mmol) at room temperature, and the solution was stirred at 60 °C until complete consumption of **2** (checked by GC). The mixture was filtered through a short pad of silica gel. After the solvents were removed under reduced pressure, the residue was purified by column chromatography on silica gel (with hexane/ethyl acetate = 95/5) followed by vacuum transfer to give the isomeric mixture of **1** (4.10 g, 72% yield) as a pale yellow oil. The *E*/*Z* ratio in **1** was determined to be 10/90 by ^{1}H NMR analysis. (*Z*)-**1**: ^{1}H NMR ($CDCl_3$) δ 2.09 (s, 3H), 4.84 (d, J = 6.0 Hz, 2H), 5.32 (d, J = 10.5 Hz, 1H), 5.66 (d, J = 16.3 Hz, 1H), 6.14 (t, J = 6.0 Hz, 1H), 6.34 (dd, J = 16.3 and 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.8, 63.8, 120.1, 128.0, 128.1, 134.9, 170.7. (*E*)-**1**: ^{1}H NMR ($CDCl_3$): δ 2.08 (s, 3H), 4.70 (d, J = 7.7 Hz, 2H), 5.46 (d, J = 10.6 Hz, 1H), 5.74 (d, J = 16.1 Hz, 1H), 6.21 (t, J = 7.7 Hz, 1H), 6.61 (dd, J = 16.1 and 10.6 Hz, 1H); EI-HRMS calcd for $C_7H_9BrO_2$ 203.9786, found 203.9789.

1,1-Bis(phenylsulfonyl)undecane (5d). To a suspension of NaH [1.1 equiv with respect to $(PhSO_2)_2CH_2$] in dry DMF (3 mL/mmol) was added solid $(PhSO_2)_2CH_2$. After hydrogen evolution had ceased, 1-iododecane [1.2 equiv with respect to $(PhSO_2)_2CH_2$] was added, and the reaction mixture was stirred at 80 °C overnight. The reaction

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mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and filtered through a short pad of silica gel. Concentration followed by recrystallization from hot MeOH afforded the pure product: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 7.1 Hz. 3H), 1.19−1.32 (br, 14H), 1.52−1.57 (m, 2H), 2.11−2.15 (m, 2H), 4.37 (t, J = 5.7 Hz. 1H), 7.57−7.60 (m, 4H), 7.68−7.73 (m, 2H), 7.95−7.98 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.2, 22.7, 25.7, 28.2, 28.97, 29.04, 29.3, 29.4, 29.5, 31.9, 83.8, 129.1, 129.7, 134.6, 137.9. Anal. Calcd for $C_{23}H_{32}O_4S_2$: C, 63.27; H, 7.39. Found: C, 63.23; H, 7.35. A molecular ion peak was not detected in a HRMS spectrum for this compound.

Palladium-Catalyzed Synthesis of Allenes 6. Preparation of allenes **6** was conducted according to a reported procedure[f] with slight modifications. The reaction conditions and the results are summarized in Table 1. A mixture of $[PdCl(\pi\text{-allyl})]_2$ (1.8 mg, 10 μmol/Pd), dpbp (5.7 mg, 11 μmol), and **1** (0.50 mmol) was dissolved in an appropriate solvent (5 mL), and the solution was added to a mixture of **5** (1.25 mmol) and base (1.25 mmol) via cannula under nitrogen. The mixture was stirred for 12 h and then filtered through a short pad of silica gel to remove precipitated inorganic salts. The silica gel pad was washed with a small amount of Et_2O three times, and the combined solution was evaporated to dryness under reduced pressure. The yellow residue was chromatographed on silica gel to give allene **6** in pure form. The characterization data of allenic products **6** are listed below.

Tetramethyl 4,5-nonadiene-2,2,8,8-tetracarboxylate (6a): ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 6H), 2.52−2.56 (m, 4H), 3.72 (s, 12H), 4.94−5.00 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 19.9, 35.8, 52.59, 52.65, 53.9, 85.3, 172.1, 172.2, 207.8; EI-HRMS calcd for $C_{17}H_{24}O_8$ 356.1471, found 356.1469. Anal. Calcd for $C_{17}H_{24}O_8$: C, 57.30; H, 6.79. Found: C, 57.12; H, 6.78.

Tetraethyl 1,7-diphenyl-3,4-heptadiene-1,1,7,7-tetracarboxylate (6b): ^{1}H NMR ($CDCl_3$) δ 1.23 (t, J = 7.1 Hz, 12H), 2.83−2.95 (m, 4H), 4.15−4.26 (m, 8H), 4.90−4.95 (m, 2H), 7.25−7.36 (m, 10H); ^{13}CNMR ($CDCl_3$): δ 14.1 (unresolved $-CO_2CH_2CH_3$), 35.7, 61.68, 61.71, 62.8, 85.8, 127.6, 128.1, 128.3, 136.5, 170.2, 170.3, 207.6; ESI-HRMS calcd for $C_{31}H_{36}O_8$ 536.2410, found 536.2405. Anal. Calcd for $C_{31}H_{36}O_8$: C, 69.39; H, 6.76. Found: C, 69.89; H, 6.79.

Tetraethyl 1,7-diacetamido-3,4-heptadiene-1,1,7,7-tetracarboxylate (6c): ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 12H), 2.05 (s, 6H), 2.97−3.00 (m, 4H), 4.21−4.29(m, 8H), 4.81−4.86(m, 2H), 6.80(s, 2H); ^{13}CNMR ($CDCl_3$): δ 13.96, 13.97, 22.9, 32.5, 62.61, 62.65, 66.2, 84.2, 167.4, 167.5, 169.1, 207.9; ESI-HRMS calcd for $C_{23}H_{34}O_{10}N_2Na$ (M + Na) 521.2111, found 521.2106. Anal. Calcd for $C_{23}H_{34}O_{10}N_2$: C, 55.41; H, 6.87; N, 5.62. Found: C, 55.34; H, 6.83; N, 5.37.

Hexaethyl 3,4-heptadiene-1,1,1,7,7,7-hexacarboxylate (6d): ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 18H), 2.74−2.88 (m, 4H), 2.97−3.00 (q, J = 7.1 Hz, 12H), 5.29−5.34(m, 2H); ^{13}CNMR ($CDCl_3$) δ 13.9, 33.1, 62.2, 65.7, 85.7, 166.5, 207.6; EI-HRMS calcd for $C_{25}H_{36}O_{12}$ 528.2207, found 528.2195. Anal. Calcd for $C_{25}H_{36}O_{12}$: C, 56.81; H, 6.87. Found: C, 56.63; H, 6.86.

1,1,7,7-Tetrakis(phenylsulfonyl)-3,4-heptadiene (6e): ^{1}H NMR ($CDCl_3$) δ 2.90 (dd, J = 7.8 and 5.9 Hz, 4H), 4.75 (t, J = 5.9 Hz, 2H), 5.30−5.35 (m, 2H), 7.51−7.56 (m, 8H), 7.64−7.70 (m, 4H), 7.90−7.97 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 24.7, 82.4, 90.2, 129.26, 129.27, 129.6, 129.9, 134.7, 134.8, 137.7, 138.1, 204.8; ESI-HRMS calcd for $C_{31}H_{28}O_8S_4Na$ (M + Na) 679.0565, found 679.0563.

11,11,17,17-Tetrakis(phenylsulfonyl)-13,14-heptacosadiene (6f): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 6H), 1.25 (br, 28H), 1.61−1.71 (m, 4H), 2.16−2.18 (m, 4H), 2.96−3.10 (m, 4H), 5.50−5.55 (m, 2H), 7.57−7.61 (m, 8H), 7.69−7.72 (m, 4H), 8.05−8.07 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 14.2, 22.8, 23.5, 28.5, 29.1, 29.38, 29.41, 29.6, 29.7, 30.4, 32.0, 85.6, 91.2, 128.7, 128.8, 131.3, 131.4, 134.7 (unresolved two diastereotopic signals), 136.9 (unresolved two diastereotopic signals), 207.4; ESI-HRMS calcd for $C_{51}H_{68}O_8S_4Na$ (M + Na) 959.3695, found 959.3698.

***N,N,N′,N′*-Tetrakis(*tert*-butoxycarbonyl)-2,3-pentadiene-1,5-diamine (6g):** ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 36H), 4.08−4.21 (m, 4H), 5.25−5.30 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.1, 45.2, 82.4, 89.5, 152.1, 205.2; ESI-HRMS calcd for $C_{25}H_{42}O_8N_2Na$ (M + Na) 521.2839, found 521.2833. Anal. Calcd for $C_{25}H_{42}O_8N_2$: C, 60.22; H, 8.49; N, 5.62. Found: C, 59.97; H, 8.44; N, 5.44.

Pd-Catalyzed Asymmetric Synthesis of (*R*)-(−)-6c. To a mixture of $Pd(dba)_2$ (7.0 mg, 12 μmol), (*R*)-segphos (8.2 mg, 13 μmol), **5c** (159 mg, 732 μmol), and CsO^tBu (126 mg, 612 μmol) in THF (3 mL) was added **1** (51.0 mg, 249 μmol) by means of syringe under nitrogen. After being stirred for 24 h at 23 °C, the mixture was filtered through a short pad of Al_2O_3 to remove precipitated inorganic salts. The Al_2O_3 pad was washed with a small amount of a hexane/EtOAc (1:1) mixture, and the combined organic solution was evaporated to dryness under reduced pressure. The residue was purified by chromatography on Al_2O_3 to give (*R*)-(−)-**6c** in pure form. Yield: 54.0 mg (44%). The enantiopurity of (*R*)-(−)-**6c** was determined to be 96% ee by chiral HPLC analysis. The absolute configuration was deduced to be (*R*) by the Lowe−Brewster rule[45,46] from the sign of optical rotation. (*R*)-(−)-**6c**: $[\alpha]^{21}_D$ = −51.8 (*c* 0.49, $CHCl_3$ for the sample of 96% ee). Chiral HPLC analysis conditions: Chiralpak AD-H; eluent, hexane/^{i}PrOH = 4/1; flow rate, 0.8 mL/min; t_1 [(*S*)-enantiomer] = 19.6 min, t_2 [(*R*)-enantiomer] = 21.4 min.

13,14-Heptacosadiene (9). Magnesium turnings (228 mg, 9.38 mmol) were placed in a Schlenk flask under nitrogen, and to this were added MeOH (5 mL) and a THF (1 mL) solution of **6d** (294 mg, 314 μmol) via syringe. The mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ether three times. The combined organic solution was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (with hexane) to give **9** (80.0 mg, 68% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 6H), 1.26−1.41 (m, 40H), 1.94−1.98 (m, 4H), 5.03−5.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.2, 22.8, 29.1, 29.2, 29.3, 29.4, 29.6, 29.736, 29.743, 29.76, 29.78, 32.0, 91.0, 203.9; EI-HRMS calcd for $C_{27}H_{52}$ 376.4069, found 376.4054.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all the new compounds and chiral HPLC chromatograms of **6c**. 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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