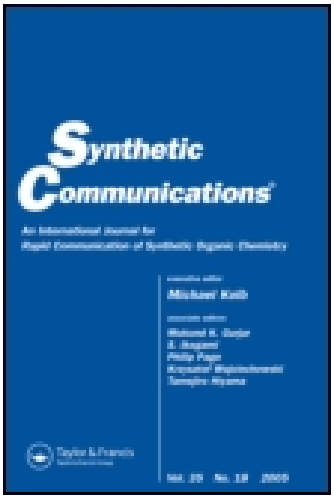


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

$PtCl_2$-Catalyzed Cyclization of o-Diethynylbenzene Derivatives Triggered by Intramolecular Nucleophilic Attack

Koji Miki [a], Hiroyuki Kuge [a], Rui Umeda [a], Motohiro Sonoda [a] & Yoshito Tobe [a]

[a] Division of Frontier Materials Science, Graduate School of Engineering Science, Osaka University, Toyonaka, Osaka, Japan

Published online: 03 Mar 2011.

To cite this article: Koji Miki, Hiroyuki Kuge, Rui Umeda, Motohiro Sonoda & Yoshito Tobe (2011) $PtCl_2$-Catalyzed Cyclization of o-Diethynylbenzene Derivatives Triggered by Intramolecular Nucleophilic Attack, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 41:7, 1077-1087, DOI: 10.1080/00397911003797817

To link to this article: http://dx.doi.org/10.1080/00397911003797817

Synthetic Communications®, 41: 1077–1087, 2011

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911003797817

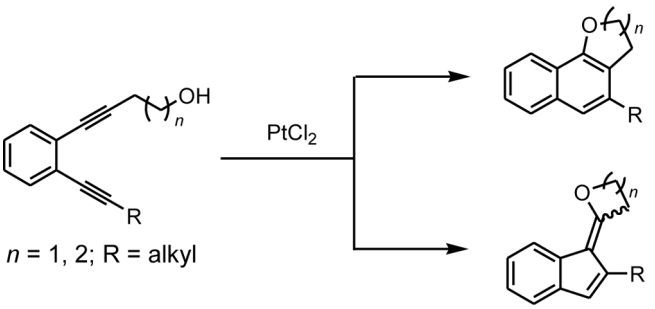
Taylor & Francis
Taylor & Francis Group

$PtCl_2$-CATALYZED CYCLIZATION OF *o*-DIETHYNYLBENZENE DERIVATIVES TRIGGERED BY INTRAMOLECULAR NUCLEOPHILIC ATTACK

Koji Miki, Hiroyuki Kuge, Rui Umeda, Motohiro Sonoda, and Yoshito Tobe

Division of Frontier Materials Science, Graduate School of Engineering Science, Osaka University, Toyonaka, Osaka, Japan

GRAPHICAL ABSTRACT



Abstract *$PtCl_2$-catalyzed cyclization of o-diethynylbenzene derivatives bearing a hydroxyethyl group yielded naphthofuran derivatives by initial intramolecular cyclization of the hydroxy group to an activated ethynyl group followed by attack of the second ethynyl group to a vinylplatinum intermediate. When the ethynyl terminal is substituted by a hydroxypropyl group, not only homologous naphthodihydropyran but also indenylidenetetrahydrofuran derivatives were formed.*

Keywords Cyclization; dihydronaphthofuran; Lewis acid; nucleophilic addition; *o*-diethynylbenzene

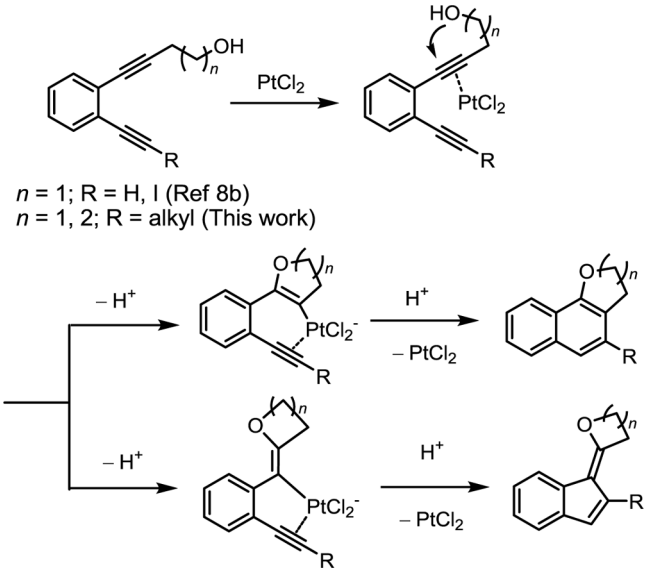
INTRODUCTION

Bergman reaction of *o*-diethynylbenzene derivatives has been recognized as one of the potential methods for preparation of naphthalene derivatives.[1] Diradical intermediates formed in this reaction can be trapped by unsaturated pendant groups, and by judicious design of substrates, polycyclic carbon skeletons can be constructed.[2] A major drawback of this method, however, is the high temperatures

Received December 19, 2009.

Address correspondence to Yoshito Tobe, Division of Frontier Materials Science, Graduate School of Engineering Science, Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan. E-mail: tobe@chem.es.osaka-u.ac.jp

required to drive the reaction if substituents of ethynyl groups are not hydrogen. Although tellurium-mediated *formal* Bergman cyclization via telluracycle intermediates has been developed by Landis et al.,[3] the scope of substrates is also limited. For enediynes bearing at least one terminal ethynyl group, transition metal–mediated cyclizations that take place via matal-vinylidene intermediates have been extensively developed.[4] For enediynes that do not bear a terminal ethynyl group, nucleophilic attack of an internal or external anionic nucleophile to a triple bond has been shown to trigger the bond formation between the triple bonds, yielding naphthalene derivatives via *formal* Bergman reactions.[5] Utimoto et al. reported intramolecular addition of alkynols catalyzed by $PdCl_2$ to furnish dihydrofuran derivatives via a 5-endo process.[6] We envisioned that the use of this reaction as a trigger of double cyclization of an *o*-diethynylbenzene bearing a hydroxyethyl group would enable the preparation of a naphthofuran derivative by attack of the second ethynyl group to the initially formed vinylplatinum intermediate through a 6-endo cyclization mode (Scheme 1).[7] Indeed, while our research was in progress, Liu et al. reported the formation of naphthodihydrofurans by $PtCl_2$-catalyzed cyclization of *o*-diethynylbenzene derivatives and proposed two types of mechanisms: one through carbene intermediates and the other via Lewis acid coordination.[8] Whereas in the Liu's reports the second ethynyl terminal groups are hydrogen or halogen, we found that substrates having an alkyl group also undergo this reaction. Moreover, when the ethynyl terminal is substituted by a hydroxypropyl group, instead of a hydroxyethyl, not only homologous naphthodihydropyran but also indenylidenetetrahydrofuran derivatives were formed. These results extend the scope and limitation of $PtCl_2$-catalyzed cyclization of *o*-diethynylbenzene derivatives triggered by intramolecular nucleophilic attack.

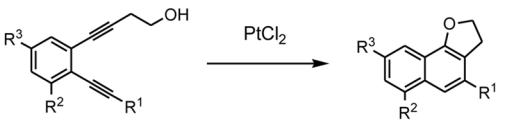


Scheme 1. $PtCl_2$-catalyzed double cyclization pathways of *o*-diethynylbenzenes.

RESULTS AND DISCUSSION

The reaction conditions were optimized using the most readily available diyne, 1,2-bis(4-hydroxybut-1-ynyl)benzene (**1a**). First, a solution of **1a** with 5 mol% of $CuCl_2$ or $PtCl_2$ was heated in chlorobenzene at 150 °C with an excess amount of 1,4-cyclohexadiene, giving naphthodihydrofuran **2a** in 34% or 56% yield, respectively. (During the initial experiments, 1,4-cyclohexadiene was added to intercept a possible diradical intermediate formed by thermal Bergman reaction. However, it turned out that even at 150 °C, no thermal reaction took place. In the subsequent experiments, therefore, cyclohexadiene was omitted.) The formation of **2a** can be interpreted in terms of an initial 5-endo cyclization followed by a 6-endo cyclization as we expected (Scheme 2). The same product was isolated when CuCl, $PdCl_2(PhCN)_2$, $Pd(OAc)_2$ (at 120 °C), or $ZnCl_2$ (at 120 °C) was used as a catalyst, but the yields of **2a** were less (<20%) because of the formation of unidentified by-products. Next, the reaction was performed by heating a toluene solution of **1a** and 5 mol% of a catalyst, $PtCl_2$, $CuCl_2$, $ZnCl_2$, $PdCl_2$(COD), or $Pd(OAc)_2$, at 80 °C. Under these conditions, only $PtCl_2$ was effective, furnishing **2a** in 41% yield. Under the same conditions, monohydroxydiyne **1b** gave the corresponding aromatization product **2b** in 76% yield. These results indicate that the alkyne units do not have to be terminated with hydrogen or halogen. Similarly, diyne **1c**, having substituents at the benzene ring, afforded the aromatization product **2c**, albeit in a lower yield (11%), presumably because of steric hindrance to the cyclization. On the other hand, phenol derivative **1d** did not react under similar conditions, indicating that phenol is not nucleophilic enough to promote the initial 5-endo cyclization. Moreover, the reaction of endiyne **3** resulted in the formation of a complex mixture of products.

Next, to investigate the effect of the length of the methylene chains on this reaction, bis(5-hydroxypent-1-ynyl)benzene (**4**) was examined. The reaction of **4** with $PtCl_2$ under similar conditions afforded naphthodihydropyran **5**, a homolog of **2a**, as the major product in 43% yield (Scheme 3). The structure of **5** was elucidated on the basis of the presence of characteristic naphthalene proton signals in the ^1H NMR spectrum, which were similar to that of **2a**. However, beside **5**, two products (**6a** and **6b**) having an indenylidenetetrahydrofuran backbone were isolated in 29 and 19% yields, respectively, and their structures were assigned mainly on the basis of ^1H NMR spectra. Namely, (*E*)-olefin **6a** exhibits the vinyl proton (Ha) signal at 6.47 ppm (s, 1H) besides aromatic proton (Hb-He) signals in the low-field region. The six methylene signals appear at 4.40 (t), 3.73 (t), 3.28 (t), 2.86 (td), 2.26 (tt), and 1.93 (tt) ppm, which are assigned to Hf to Hk shown in Scheme 3. The stereochemistry of the double bond was determined on the basis on the nuclear Overhauser



1a $R^1 = CH_2CH_2OH$, $R^2 = R^3 = H$
1b $R^1 = n$-Bu, $R^2 = R^3 = H$
1c $R^1 = n$-Bu, $R^2 = Br$, $R^3 = t$-Bu

2a $R^1 = CH_2CH_2OH$, $R^2 = R^3 = H$
2b $R^1 = CH_2CH_3$, $R^2 = R^3 = H$
2c $R^1 = CH_2CH_3$, $R^2 = Br$, $R^3 = t$-Bu

Scheme 2. $PtCl_2$-catalyzed cyclization of *o*-diethynylbenzenes.

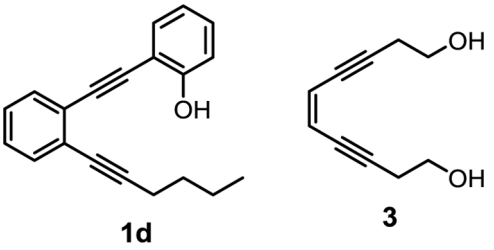
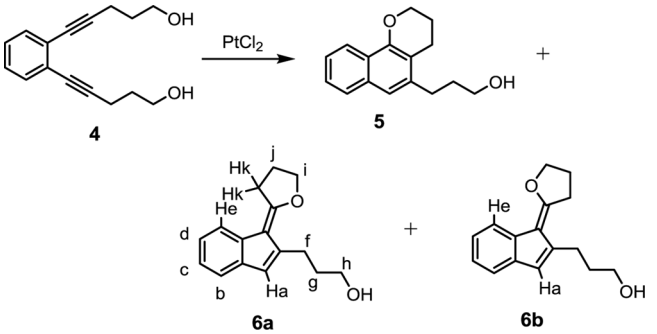


Figure 1. Structures of substrates **1d** and **3**.



Scheme 3. $PtCl_2$-catalyzed cyclization of *o*-diethynylbenzene **4**.

effect (NOE): Correlation was observed between He and Hk, indicating that these protons are located in close proximity. The ^{1}H NMR signals of the diastereomer **6b** are similar to those of **6a** except for the aromatic proton He (7.99–8.04 ppm): It appears distinctly downfield relative to that of **6a** (7.36–7.40 ppm) owing to the deshielding effect of the proximate oxygen atom of the furan ring, indicating the *Z* stereochemistry of the exocyclic double bond. The formation of both *E* and *Z* isomers is ascribed to an equilibrium, because leaving a $CDCl_3$ solution of either **6a** or **6b** at room temperature for a few days led to the formation of an equilibrium mixture of them. (A small amount of unidentified product also formed during the equilibration.)

The formation of **5** is explained in terms of sequential 6-endo cyclizations as described previously. On the other hand, furan derivatives **6a** and **6b** are formed by initial 5-exo followed by second 5-endo cyclizations. Thus the second cyclization mode is related to the first one, because the position of the nucleophilic center in the intermediate, at either benzylic or homobenzylic position, is governed by the mode of the first step. Elongation of the methylene units allowed two modes of the initial cyclization step to occur because of increased flexibility of the methylene chains.

CONCLUSIONS

$PtCl_2$-catalyzed cyclization of *o*-diethynylbenzene derivatives bearing a hydroxyethyl group gave naphthofuran derivatives by initial 5-endo followed by 6-endo

cyclizations. On the other hand, the reaction of an *o*-diethynylbenzene derivative bearing a hydroxypropyl group yielded not only naphthodihydropyran via sequential 6-endo cyclizations but also indenylidenetetrahydrofuran derivatives via tandem 5-exo followed by 5-endo cyclizations. These results extend the scope and limitation of $PtCl_2$-catalyzed aromatization of *o*-diethynylbenzene derivatives triggered by intramolecular nucleophilic attack.

EXPERIMENTAL

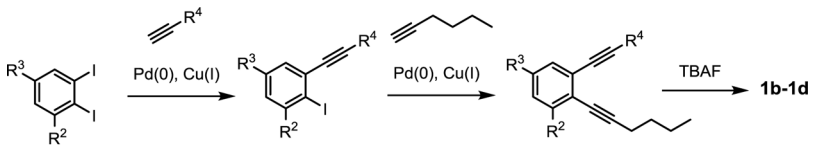
^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300, a JEOL JNM-GSX-270, or a JEOL JNM AL-400 spectrometer in $CDCl_3$ and with Me_4Si or residual solvent as an internal standard at 30 °C. Infrared (IR) spectra were taken with a JASCO Fourier transform (FT)/IR-410 spectrometer, and mass spectra were obtained on a JEOL JMS-700 spectrometer. Preparative GPC separation was undertaken with a JAI LC-908 chromatograph using 600 mm × 20 mm JAIGEL-1H and 2H gel permeation chromatography (GPC) columns with $CHCl_3$ as an eluent. All reagents were obtained from commercial suppliers and used as received. Solvents were dried (drying agent in parentheses) and distilled prior to use: Tetrahydrofuran (THF) (sodium benzophenone ketyl), diethylamine (KOH), piperidine (KOH), and toluene (CaH_2).

General Procedure for the Pd-Cu–Catalyzed Coupling Reaction (GP1)

An acetylene derivative was added to a solution of an aromatic iodide, $Pd(PPh_3)_4$, and CuI in solvent and/or amine under an argon atmosphere at the indicated temperature. After being stirred for the indicated time, 1 N aqueous HCl was added, and the reaction mixture was extracted with $CHCl_3$. The organic layer was washed with saturated aqueous $NaHCO_3$ and dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue was passed through a silica-gel column followed by preparative GPC to afford the coupling product.

General Procedure for the Pt-Catalyzed Cyclization (GP2)

A solution of $PtCl_2$ (5 mol%) and diyne **1** in toluene (1.0 mL) was stirred for the indicated time under an argon atmosphere at 80 °C. After removal of the solvent



7b, **8b** $R^2 = R^3 = H$, $R^4 = CH_2CH_2OTBDMS$
7c, **8c** $R^2 = Br$, $R^3 = t\text{-Bu}$, $R^4 = CH_2CH_2OTBDMS$
7d, **8d** $R^2 = R^3 = H$, $R^4 = 2\text{-TBDMSO-}C_6H_4$

Scheme 4. Preparation of diynes **1b–d**.

under reduced pressure, the residue was purified on a silica-gel column to give dihydronaphthofuran derivative **2**.

Synthesis of Diyne 1a

Compound **1a** was obtained using *o*-diiodobenzene (0.33 g, 1.0 mmol), 3-butyn-1-ol (175 mg, 2.50 mmol), $Pd(PPh_3)_4$ (11 mg, 9.5 μmol), CuI (4 mg, 0.02 mmol), and piperidine (1.0 mL) by applying GP1 (reaction time: 18 h, reaction temperature: rt) in 76% yield (163 mg) as a yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40 and 7.22 (AA′BB′, $J_{AB} = 7.2$, $J_{AB'} = 1.4$ Hz, 4H), 3.82 (t, $J = 6.0$ Hz, 4H), 2.74 (t, $J = 6.0$ Hz, 4H), 2.23 (brs, 2H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 131.5, 127.4, 125.7, 90.7, 81.5, 60.7, 24.0. IR (neat) 3356, 2884, 2233, 1929, 1822, 1635, 1592, 1480, 1442, 1332, 1291, 1186, 1105, 1040, 950, 877, 846, 758 cm^{-1}. MS (EI) m/z 214 (M^+). HRMS (EI) calcd. for $C_{14}H_{14}O_2$: 214.0994. Found: 214.0974.

$PtCl_2$-Catalyzed Cyclization of 1a: Synthesis of Dihydronaphthofuran 2a

Dihydronaphthofuran **2a** was obtained using **1a** (53.3 mg, 0.25 mmol) and $PtCl_2$ (3.3 mg, 0.013 mmol) by applying GP2 (reaction time: 1 h) in 41% yield (21.6 mg) as a white solid. Mp 64–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93–7.89 (m, 1H), 7.78–7.72 (m, 1H), 7.44–7.36 (m, 2H), 7.21 (s, 1H), 4.76 (t, $J = 9.0$ Hz, 2H), 3.90 (t, $J = 6.6$ Hz, 2H), 3.30 (t, $J = 9.0$ Hz, 2H), 2.95 (t, $J = 6.6$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 134.0, 133.0, 127.2, 125.7, 124.6, 121.2, 119.9, 119.4, 119.3, 71.7, 62.3, 37.1, 29.5. IR (KBr) 3312, 2961, 1596, 1571, 1519, 1401, 1386, 1341, 1284, 1072, 942, 924, 841, 749, 608, 527 cm^{-1}. MS (EI) m/z 214 (M^+). HRMS (EI) calcd. for $C_{14}H_{14}O_2$: 214.0994. Found: 214.0982.

Synthesis of Diyne 1b

Compound **7b** was obtained using *o*-diiodobenzene (3.03 g, 9.2 mmol), 1-(*tert*-butyldimethylsilyloxy)but-3-yne (1.65 g, 8.95 mmol), $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol), CuI (0.14 g, 0.75 mmol), and piperidine (5.0 mL) by applying GP1 (reaction time: 18 h, reaction temperature: rt) in 42% yield (1.5 g) as a yellow oil together with a disubstitution product (0.29 g, 7% yield) as a yellow oil.

Compound **7b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.40 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.26 (ddd, $J = 7.5$, 7.5, 1.5 Hz, 1H), 6.95 (ddd, $J = 7.5$, 7.5, 1.5 Hz, 1H), 3.87 (t, $J = 7.2$ Hz, 2H), 2.70 (t, $J = 7.2$ Hz, 2H), 0.92 (s, 9H), 0.11 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 132.4, 130.2, 128.7, 127.6, 100.9, 91.4, 83.8, 61.8, 26.0, 24.1, 18.4, −5.1. IR (neat) 2955, 2929, 2857, 2231, 1472, 1385, 1254, 1106, 915, 837, 777, 756, 661 cm^{-1}.

Disubstitution product: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, $J = 5.7$, 3.6 Hz, 2H), 7.18 (dd, $J = 5.7$, 3.6 Hz, 2H), 3.85 (t, $J = 7.5$ Hz, 4H), 2.68 (t, $J = 7.5$ Hz, 4H), 0.92 (s, 18H), 0.10 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$, 30 °C) δ 131.7, 127.2, 126.1, 90.7, 80.5, 62.1, 26.0, 24.2, 18.4, −5.1. MS (EI) m/z 442 (M^+). HRMS (EI) calcd. for $C_{26}H_{42}O_2Si_2$: 442.2723. Found: 442.2718.

Compound **8b** (0.34 g) was obtained using **7b** (0.39 g, 1.0 mmol), 1-hexyne (180 mg, 2.2 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), CuI (14 mg, 0.075 mmol), Et_2NH (0.5 mL), and toluene (2.0 mL) by applying GP1 (reaction time: 3.5 h, reaction temperature: rt). The crude product was used in the next step without further purification.

A solution of tetra-n-butylammonium fluoride (TBAF) (1 M in THF, 1.2 mL, 1.2 mmol) was added dropwise to a solution of the crude **8b** (0.34 g) in THF (2.0 mL) at room temperature under a nitrogen atmosphere. After being stirred for 15 min, the solvent was removed under reduced pressure. The residue was subjected to chromatography on silica gel (*n*-hexane/AcOEt 4:1 to 1:1) to give **1b** (0.21 g, 93% for two steps) as a yellow oil.

Compound **1b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.41 (m, 2H), 7.18–7.23 (m, 2H), 3.82 (t, $J = 6.0$ Hz, 2H), 2.74 (t, $J = 6.0$ Hz, 2H), 2.48 (t, $J = 6.9$ Hz, 2H), 1.92 (br s, 1H), 1.45–1.67 (m, 4H), 0.96 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 30 °C) δ 131.8, 131.4, 127.5, 127.1, 126.6, 125.3, 94.4, 89.9, 82.1, 79.7, 61.0, 30.9, 24.2, 22.1, 19.4, 13.8. IR (neat) 3389, 2957, 2932, 2872, 2231, 1480, 1442, 1046, 758 cm^{-1}. MS (EI) m/z 226 (M^+). HRMS (EI) calcd. for $C_{16}H_{18}O$: 226.1358. Found: 226.1381.

$PtCl_2$-Catalyzed Cyclization of 1b: Synthesis of Dihydronaphthofuran 2b

Dihydronaphthofuran **2b** was obtained using **1b** (22.3 mg, 0.10 mmol), $PtCl_2$ (26.8 mg, 0.10 mmol), and toluene (1.0 mL) by applying GP2 (reaction time: 40 h) in 76% yield (16.9 mg) as a white solid. Mp 60–61 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93–7.89 (m, 1H), 7.78–7.73 (m, 1H), 7.42–7.34 (m, 2H), 7.18 (s, 1H), 4.79 (t, $J = 8.8$ Hz, 2H), 3.34 (t, $J = 8.8$ Hz, 2H), 2.72 (t, $J = 7.6$ Hz, 2H), 1.68 (tt, $J = 7.6$, 7.6 Hz, 2H), 1.44 (qt, $J = 7.6$, 7.6 Hz, 2H), 0.98 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 137.6, 134.3, 127.3, 125.6, 124.3, 121.3, 119.9, 119.1, 118.5, 71.7, 33.6, 32.2, 29.5, 22.6, 14.0. IR (KBr): 3047, 2951, 2924, 2856, 1593, 1514, 1387, 1284, 1066, 1048, 1012, 982, 918, 843, 750, 736, 576 cm^{-1}. MS (EI) m/z 226 (M^+). HRMS (EI) calcd. for $C_{16}H_{18}O$: 226.1358. Found: 226.1342.

Synthesis of Diyne 1c

Compound **7c** was obtained using 5-*tert*-butyl-1-bromo-2,3-diiodobenzene[2c] (909 mg, 1.95 mmol), 1-(*tert*-butyldimethylsilyloxy)but-3-yne (437 mg, 2.37 mmol), $Pd(PPh_3)_4$ (33.0 mg, 28.6 μmol), CuI (27.0 mg 142 μmol), and piperidine (3.0 mL) by applying GP1 (reaction time: 20 h, reaction temperature: 60 °C) in 87% yield (885 mg) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, $J = 2.1$ Hz, 1H), 7.34 (d, $J = 2.1$ Hz, 1H), 3.87 (t, $J = 6.9$ Hz, 2H), 2.71 (t, $J = 6.9$ Hz, 2H), 1.28 (s, 9H), 0.92 (s, 9H), 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 129.0, 128.0, 127.9, 125.5, 102.6, 91.4, 80.4, 62.0, 34.8, 30.8, 25.9, 24.0, 18.3, −0.0, −5.2.

Compound **8c** was obtained using **7c** (260 mg, 499 μmol), 1-hexyne (56 mg, 680 μmol), $Pd(PPh_3)_4$ (25.0 mg, 21.6 μmol), CuI (50.4 mg, 264 μmol), and piperidine (3.0 mL) by applying GP1 (reaction time: 20 h, reaction temperature: 60 °C) in 43% yield (103 mg) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, $J = 2.1$ Hz, 1H),

7.34 (d, $J = 2.1$ Hz, 1H), 3.85 (t, $J = 7.5$ Hz, 2H), 2.68 (t, $J = 7.5$ Hz, 2H), 2.52 (t, $J = 7.5$ Hz, 2H), 1.70–1.48 (m, 4H), 1.27 (s, 9H), 0.96 (t, $J = 7.2$ Hz, 3H), 0.92 (s, 9H), 0.10 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3, 128.9, 127.9, 127.8, 125.4, 124.4, 102.4, 102.0, 91.3, 80.4, 62.0, 34.7, 31.0, 30.8, 26.0, 24.1, 22.0, 19.6, 18.4, 0.11, −5.1. IR (neat) 2957, 2857, 2232, 1590, 1529, 1462, 1397, 1362, 1255, 1208, 1106, 1058, 1006, 913, 836, 777, 665 cm^{-1}. MS (EI) m/z 474 (M^+).

A solution of TBAF (1 M in THF, 1.0 mL, 1.0 mmol) was added dropwise to a solution of **8c** (106 mg, 223 μmol) in THF (3.0 mL) at 0 °C under a nitrogen atmosphere. After being stirred for 1 h, water was added to the reaction mixture, and the mixture was extracted with $CHCl_3$. The organic layer was washed with brine and dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue was subjected to chromatography on silica gel (*n*-hexane/AcOEt 2:1) followed by preparative GPC to afford **1c** (68.1 mg, 85%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, $J = 1.8$ Hz, 1H), 7.35 (d, $J = 1.8$ Hz, 1H), 3.81 (t, $J = 5.4$ Hz, 2H), 2.73 (t, $J = 6.0$ Hz, 2H), 2.52 (t, $J = 6.9$ Hz, 2H), 2.17 (brs, 1H), 1.69–1.48 (m, 4H), 1.27 (s, 9H), 0.96 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.4, 129.1, 127.5, 126.7, 125.4, 125.3, 98.6, 90.1, 82.0, 78.8, 60.9, 34.7, 31.0, 30.7, 24.2, 22.0, 19.5, 13.7. IR (neat) 3397, 2960, 2933, 2871, 2230, 1718, 1590, 1528, 1455, 1397, 1178, 1048, 874, 647 cm^{-1}. MS (EI) m/z 360 (M^+). HRMS (EI) calcd. for $C_{16}H_{17}O^{79}Br$: 360.1089. Found: 360.1076.

$PtCl_2$-Catalyzed Cyclization of 1c

Dihydronaphthofuran **2c** was obtained using **1c** (36.1 mg, 100 μmol), $PtCl_2$ (3.0 mg, 11 μmol), and toluene (1.0 mL) by applying GP2 (reaction time: 24 h) in 11% yield (4.0 mg) as a white solid. Mp 119–120 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, $J = 1.8$ Hz, 1H), 7.76 (d, $J = 1.8$ Hz, 1H), 7.48 (s, 1H), 4.80 (t, $J = 9.0$ Hz, Hz, 2H), 3.34 (t, $J = 9.0$ Hz, 2H), 2.72 (t, $J = 7.8$ Hz, 2H), 1.71–1.41 (m, 4H), 1.38 (s, 9H), 0.97 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 138.2, 130.8, 129.5, 128.8, 128.7, 122.2, 120.9, 117.7, 116.2, 72.0, 35.0, 34.0, 32.4, 31.3, 29.5, 22.7, 14.1. IR (KBr) 2958, 2928, 2860, 1597, 1496, 1463, 1416, 1375, 1311, 1281, 1253, 1208, 1059, 965, 874, 755, 618 cm^{-1}. MS (EI) m/z 360 (M^+). HRMS (EI) calcd. for $C_{20}H_{25}O^{79}Br$: 360.1089. Found: 360.1101.

Synthesis of Diyne 1d

Compound **7d** was obtained using *o*-diiodobenzene (3.79 g, 1.2 mmol), (2-ethynylphenoxy)-*tert*-butyldimethylsilane[9] (2.3 g, 10 mmol), $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol), CuI (0.14 g, 0.75 mmol), and piperidine (5.0 mL) by applying GP1 (reaction time: 30 min, reaction temperature: rt) in 36% yield (1.5 g) as a yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.92–7.85 (m, 1H), 7.59 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.50 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.32 (ddd, $J = 7.6$, 7.6, 1.1 Hz, 1H), 7.27–7.20 (m, 1H), 7.06–6.93 (m, 2H), 6.89–6.84 (m, 1H), 1.05 (s, 9H), 0.28 (s, 6H).

Compound **8d** (0.52 g) was obtained using **7d** (0.65 g, 1.5 mmol), 1-hexyne (164 mg, 2.00 mmol), $Pd(PPh_3)_4$ (43 mg, 0.037 mmol), CuI (21 mg, 0.11 mmol), and piperidine (2.0 mL) by applying GP1 (reaction time: 30 min, reaction temperature: rt). The crude product was used in the next step without further purification.

A solution of TBAF (1 M in THF, 1.2 mL, 1.2 mmol) was added dropwise to a solution of **8d** (0.52 g) in THF (5.0 mL) at 0 °C under a nitrogen atmosphere. After being stirred for 15 min, the solvent was removed under reduced pressure. The residue was subjected to chromatography on silica gel (*n*-hexane/AcOEt 50:1) to give **1d** (0.23 g, 56% for two steps) as a yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.53–7.47 (m, 2H), 7.42 (dd, $J = 5.1$, 1.1 Hz, 2H), 7.30–7.25 (m, 2H), 7.00 (d, $J = 5.7$ Hz, 1H), 6.92–6.89 (m, 1H), 6.57 (brs, 1H), 2.56 (t, $J = 4.9$ Hz, 2H), 1.65 (tt, $J = 4.9$, 4.9 Hz, 2H), 1.50 (qt, $J = 4.9$, 4.9 Hz, 2H), 0.94 (t, $J = 4.9$, 4.9 Hz, 3H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 157.2, 132.2, 130.9, 130.9, 130.6, 128.3, 127.5, 126.3, 124.7, 120.1, 114.6, 109.5, 95.9, 95.6, 87.0, 80.0, 25.6, 22.1, 19.3, 13.6. IR (neat) 3456, 3061, 2957, 2931, 2871, 2210, 1574, 1490, 1474, 1347, 1291, 1241, 1195, 1144, 806, 753 cm^{-1}. MS (EI) m/z 226 (M^+). HRMS (EI) calcd. for $C_{20}H_{18}O$: 274.1358. Found: 274.1360.

Synthesis of Diyne 3

Compound **3** was obtained using 1,2-dichloroethylene (291 mg, 3.0 mmol), 3-butyn-1-ol (537 mg, 7.66 mmol), $Pd(PPh_3)_4$ (0.17 g, 0.15 mmol), CuI (86 mg, 0.45 mmol), Et_2NH (3.1 mL), and toluene (5.0 mL) by applying GP1 (reaction time: 24 h, reaction temperature: rt) in 56% yield (0.28 g) as a yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.78 (s, 2H), 3.75 (t, $J = 5.9$ Hz, 4H), 2.66 (t, $J = 5.9$ Hz, 4H), 2.49 (brs, 2H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 119.5, 94.5, 80.4, 60.7, 24.1. IR (neat) 3364, 2944, 2887, 2216, 1419, 1043, 848, 750 cm^{-1}. MS (EI) m/z 164 (M^+). HRMS (EI) calcd. for $C_{10}H_{12}O_2$: 164.0837. Found: 164.0816.

Synthesis of Diyne 4

Compound **4** was obtained using *o*-diiodobenzene (0.99 g, 3.0 mmol), 4-pentyn-1-ol (606 mg, 7.2 mmol), $Pd(PPh_3)_4$ (0.17 g, 0.15 mmol), CuI (86 mg, 0.45 mmol), Et_2NH (3.1 mL), and toluene (5.0 mL) by applying GP1 (reaction time: 24 h, reaction temperature: rt) in 86% yield (0.63 g) as a yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.37 (dd, $J = 5.7$, 3.5 Hz, 2H), 7.19 (dd, $J = 5.7$, 3.5 Hz, 2H), 3.85 (t, $J = 6.2$ Hz, 4H), 2.70 (brs, 2H), 2.61 (t, $J = 6.2$ Hz, 4H), 1.86 (tt, $J = 6.2$, 6.2 Hz, 4H). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 131.9, 127.4, 126.0, 93.2, 80.3, 61.5, 31.2, 16.2. IR (neat) 3349, 2947, 2226, 1480, 1442, 1058, 958, 924, 759 cm^{-1}. MS (FAB) m/z 243 ($M + H^+$). HRMS (FAB) calcd. for $C_{16}H_{19}O_2$: 243.1385. Found: 243.1380.

$PtCl_2$-Catalyzed Cyclization of 4

The reaction of **4** (61 mg, 0.25 mmol), $PtCl_2$ (3.3 mg, 0.013 mmol), and toluene (1.0 mL) by applying GP2 (reaction time: 2 h) gave dihydronaphthofuran **5** in 43% yield (26 mg) as a white solid together with indenylidenetetrahydrofurans **6a** (18 mg, 29%) and **6b** (12 mg, 19%) both as yellow solids.

Compound **5**: mp 62–63 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.13–8.10 (m, 1H), 7.68–7.66 (m, 1H), 7.41–7.37 (m, 2H), 7.21 (s, 1H), 4.35 (t, $J = 5.1$ Hz, 2H), 3.77 (t, $J = 6.2$ Hz, 2H), 2.85 (t, $J = 6.5$ Hz, 2H), 2.79 (t, $J = 7.8$ Hz, 2H), 2.14 (tt, $J = 6.5$, 5.1 Hz, 2H), 1.94 (tt, $J = 7.8$, 6.2 Hz, 2H), 1.62 (s, 1H). ^{13}C NMR

(67.5 MHz, $CDCl_3$) δ 150.1, 138.9, 132.8, 126.8, 125.7, 124.4, 124.1, 121.4, 118.5, 115.3, 66.1, 62.6, 32.9, 29.0, 22.5, 22.2. IR (KBr) 3326, 3070, 3048, 2964, 2926, 2873, 1706, 1634, 1598, 1497, 1471, 1446, 1404, 1323, 1282, 1177, 1116, 1078, 1053, 956, 919, 906, 738 cm^{-1}. MS (EI) m/z 242 (M^+). HRMS (EI) calcd. for $C_{16}H_{18}O_2$: 242.1307. Found: 242.1309.

Compound **6a**: mp 92–93 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.40 (m, 1H), 7.28 (dd, $J = 7.2$, 1.6 Hz, 1H), 7.13 (ddd, $J = 7.2$, 7.2, 1.6 Hz, 1H), 7.09 (ddd, $J = 7.2$, 7.2, 1.6 Hz, 1H), 6.47 (s, 1H), 4.40 (t, $J = 7.2$ Hz, 2H), 3.73 (t, $J = 6.4$ Hz, 2H), 3.28 (t, $J = 7.6$ Hz, 2H), 2.86 (td, $J = 7.6$, 1.0 Hz, 2H), 2.26 (tt, $J = 7.6$, 7.2 Hz, 2H), 1.93 (tt, $J = 7.6$, 6.4 Hz, 2H), 1.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 142.1, 141.3, 136.8, 124.3, 122.8, 122.7, 120.2, 119.9, 113.0, 72.0, 63.0, 32.7, 31.2, 27.2, 23.8. IR (KBr) 3316, 3089, 3059, 2934, 2902, 2872, 1707, 1632, 1455, 1181, 1045, 997, 752 cm^{-1}. MS (EI) m/z 242 (M^+). HRMS (EI) calcd. for $C_{16}H_{18}O_2$: 242.1307. Found: 242.1331.

Compound **6b**: mp 69–72 °C. ^1H NMR (270 MHz, $CDCl_3$) δ 7.99–8.04 (m, 1H), 7.25 (dd, $J = 6.5$, 1.8 Hz, 1H), 7.10–7.15 (m, 2H), 6.46 (s, 1H), 4.46 (t, $J = 6.8$ Hz, 2H), 3.79 (t, $J = 6.5$ Hz, 2H), 3.17 (t, $J = 7.6$ Hz, 2H), 2.72 (td, J = 6.8, 1.0 Hz, 2H), 2.23 (tt, $J = 6.8$, 6.8 Hz, 2H), 1.96 (tt, $J = 7.6$, 6.5 Hz, 2H), 1.56 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 140.9, 140.2, 135.6, 124.8, 123.5, 123.2, 122.7, 119.2, 113.7, 71.7, 62.6, 32.2, 30.5, 26.5, 24.3. IR (KBr) 3344, 3071, 3041, 2940, 2867, 1709, 1644, 1450, 1189, 1019, 930, 858, 766, 737 cm^{-1}. MS (EI) m/z 242 (M^+). HRMS (EI) calcd. for $C_{16}H_{18}O_2$: 242.1307. Found: 242.1284.

ACKNOWLEDGMENT

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

REFERENCES

1. For reviews, see (a) Wang, K. K. Cascade radical cyclization via biradicals generated from enediynes, enyne-allenes, and enyne-ketenes. *Chem. Rev.* **1996**, *96*, 207–222; (b) Basak, A.; Mandal, S.; Bag, S. S. Chelation-controlled Bergman cyclization: Synthesis and reactivity of enediynyl ligands. *Chem. Rev.* **2003**, *103*, 4077–4094.
2. (a) Grisson, J. W.; Calkins, T. L.; Egan, M. Synthetic studies of the tandem enediyne-mono- and bis-radical cyclizations. *J. Am. Chem. Soc.* **1993**, *115*, 11744–11752; (b) Grisson, J. W.; Calkins, T. L.; Huang, D.; McMillen, H. High temperature radical cyclization anomalies in the tandem enediyne-*bis*-radical cyclization. *Tetrahedron* **1994**, *50*, 4635–4650; (c) Chow, S.-Y.; Palmer, G. J.; Bowles, D. M.; Anthony, J. E. Perylene synthesis by the parallel cycloaromatization of adjacent endiynes. *Org. Lett.* **2000**, *2*, 961–963; (d) Bowles, D. M.; Palmer, G. J.; Landis, C. A.; Scott, J. L.; Anthony, J. E. The Bergman reaction as a synthetic tool: Advantages and restrictions. *Tetrahedron* **2001**, *57*, 3753–3760; (e) Scott, J. L.; Pakin, S. R.; Anthony, J. E. Radical-induced cycloaromatization: Routes to fluoranthenes and acephenanthrylenes. *Synlett* **2004**, 161–164.
3. Landis, C. A.; Payne, M. M.; Eaton, D. L.; Anthony, J. E. Tellurium-mediated cycloaromatization of acyclic endiynes under mild conditions. *J. Am. Chem. Soc.* **2004**, *126*, 1338–1339.

4. (a) Wang, Y.; Finn, M. G. An organometallic diradical cycloaromatization reaction. *J. Am. Chem. Soc.* **1995**, *117*, 8045–8046; (b) Ohe, K.; Kojima, M.-A.; Yonehara, K.; Uemura, S. Rhodium(I)-catalyzed cycloaromatization of acyclic 3-ene-1,5-diynes. *Angew. Chem. Int. Ed.* **1996**, *35*, 1823–1825; (c) Manabe, T.; Yanagi, S.-I.; Ohe, K.; Uemura, S. New examples of 1,6- and 1,7-hydrogen transfer promoted by an α-silyl group in rhodium(I)-catalyzed radical reactions of acyclic enediynes. *Organometallics* **1998**, *17*, 2942–2944; For reviews, see (d) König, B. Changing the reactivity of enediynes by metal-ion coordination. *Eur. J. Org. Chem.* **2000**, 381–385; (e) Trost, B. M.; McClory, A. Metal vinylidenes as catalytic species in organic reactions. *Chem. Asian J.* **2008**, *3*, 164–194.
5. (a) Wu, M.-J.; Lee, C.-Y.; Lin, C.-F. A route to 5-substituted dibenzofurans by anionic cycloaromatization of 2-(6-substituted 3-hexen-1,5-diynyl)phenyl *tert*-butyldimethyl ethers and related molecules. *Angew. Chem. Int. Ed.* **2002**, *41*, 4077–4079; (b) Wu, M.-J.; Lin, C.-F.; Lu, W.-D. Anionic cycloaromatization of 1-aryl-3-hexen-1,5-diynes initiated by methoxide addition: Synthesis of phenanthridinones, benzo[*c*]phenanthridinones, and biaryls. *J. Org. Chem.* **2002**, *67*, 5907–5912.
6. (a) Utimoto, K. Palladium-catalyzed synthesis of heterocycles. *Pure Appl. Chem.* **1983**, *55*, 1845–1852; (b) Wakabayashi, Y.; Fukuda, Y.; Shiragami, H.; Utimoto, K.; Nozaki, H. Preparation of furans from alkynols utilyzing palladium-catalyzed intramolecular addition of alcohols to acetylene as a key reaction. *Tetrahedron* **1985**, *41*, 3655–3661.
7. Kuge, H.; Miki, K.; Sonoda, M.; Tobe, Y. Synthesis of dihydronaphthofuran derivatives via tandem cyclization of diethynylbenzene. Paper presented at the 86th annual meeting of the Chemical Society of Japan, 27–30, March 2006.
8. (a) Taduri, B. P.; Ran, Y. F.; Huang, C.-W.; Liu, R.-S. Platinum-catalyzed aromatization of endiynes via a C−H bond insertion of tethered alkanes. *Org. Lett.* **2006**, *8*, 883–886; (b) Taduri, B. P.; Odedra, A.; Lung, C.-Y.; Liu, R.-S. Platinum- and ruthenium-catalyzed aromatization of endiynes via intramolecular nucleophilic additions. *Synthesis* **2007**, 2050–2054; For a review, see (c) Liu, R.-S. Catalytic transformations of terminal alkynes by cationic tris(1-propazolyl)borate ruthenium catalysts: Versatile chemistry via catalytic allenylidene, vinylidene, and π–alkyne intermediates. *Synlett* **2008**, 801–812.
9. Vedejs, E.; Steck, P. L. Unusual oxaphosphoranes by acyl transfer from *o*-acetoxy-*o*′-diphenylphosphanyltolane. *Angew. Chem. Int. Ed.* **1999**, *38*, 2788–2791.